University of Alberta

HYPOALGESIC EFFECTS OF INTERFERENTIAL CURRENT THERAPY ON PRESSURE PAIN THRESHOLDS (PPT) IN HEALTHY SUBJECTS

by

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A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of

Master of Science
in
Rehabilitation Science - Physical Therapy

Department of Physical Therapy

Edmonton, Alberta
Fall 2007

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Your file Votre référence
ISBN: 978-0-494-33242-9
Our file Notre référence
ISBN: 978-0-494-33242-9

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DEDICATION

To Andrea and Maximiliano for inspiring me. To my father, who taught me the values to success in the life and helped me to appraise the meaning of the family. Although he is no longer with us, he will be for ever remembered. I am sure he shares my happiness in the heaven

ABSTRACT

Interferential current (IFC) is a popular type of transcutaneous electrical nerve stimulation used to control pain. Despite the profuse use of IFC in clinical practice, its effectiveness is controversial. Amplitude-modulated frequency (AMF) or the "beat frequency" parameter has been traditionally considered an effective component of IFC. However, recent evidence questions the importance of the AMF component in its therapeutic effects. The aims of this study were to investigate the hypoalgesic effects of IFC on an experimentally-induced mechanical pain model in normal subjects, and to describe and compare its effectiveness on pressure pain threshold using two different settings of AMF parameter (100 Hz and 0 Hz) in healthy males and females.

Based on the results obtained from this study, IFC showed; firstly a hypoalgesic effect in increasing the pressure pain thresholds in healthy subjects. Secondly, the application of different settings of AMF did not influence the hypoalgesic response.

ACKNOWLEDGMENTS

I would like to thank the many people who contributed in some way to this thesis. Firstly, I would like to express my deep and sincere gratitude to my supervisor, Dr. David Magee for his knowledge, enduring support, willingness and personal guidance throughout this time. I would also gratefully acknowledge to my committee, Dr. Sharon Warren and Dr. Douglass Gross for their helpful comments, orientation and valuable feedback.

I would like to say a big thank you to all the people who agreed to voluntarily participate in my research and provided me with the experimental data.

Thanks also go to all my research's helpers, Na, Luciana and Susan for generously sharing their time. I would have been lost without their logistic help. In particular, a big thanks to my friend Susan for helping me gets through the difficult times and her constructive criticism.

In addition, I would also like to express my love and gratitude to my mother, Carmen; my father, Jorge; and brothers, Cristian and Nelson for their unconditional and continuous support, through overseas phone calls, and for encouraging me during this endeavor.

Finally, I cannot end without thanking those closest to me, my beloved wife Andrea, for her understanding, endless patience, and encouragement and for always supporting me in my dreams and aspirations, Maximiliano, my son, for transmitting me his happiness and for surprising me every day.

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CHAPTER ONE: INTRODUCTION

1.1 INTRODUCTION AND PROBLEM STATEMENT

Pain is a complex phenomenon due to its complicated neurophysiological basis, its emotional connotations and its inherent subjectivity. In the same way, the spectrum of alternatives to control painful conditions is wide, including the use of drugs, electrophysical agents, and alternative medicine, among others.

The use of physical agents based on electrical currents for pain relief dates as far back as the Egyptian Fifth Dynasty (Alves-Guerreiro *et al.* 2001). However, with the publication of the pain gate theory (Melzack & Wall 1965), the theoretical fundamentals of the use of the electrical currents for pain relief have become more widely accepted. Currently, therapeutic current modalities have become increasingly popular as non-pharmacological alternatives to relieve pain in both acute and chronic conditions (Quirk *et al.* 1985; Taylor *et al.* 1987; Checchia *et al.* 1991; Werners *et al.* 1999; Hurley *et al.* 2001, 2004; Almeyda *et al.* 2003; Jarit *et al.* 2003; Atamaz *et al.* 2006). Interferential Current Therapy (IFC) is the transcutaneous application of alternating medium-frequency electrical current (normally 4000Hz) amplitude modulated at low frequency (0 to 250 Hz) for therapeutic purposes (Nikolova 1987; Low & Reed 2000; Palmer& Martin 2002). Amplitude-modulated frequency (AMF) or the "beat frequency" parameter has been traditionally considered an effective component of IFC (Wodsworth & Chanmugam 1983; Goats 1990; Low & Reed 1990, 2000; Kloth 1992). This low frequency (AMF) could produce the stimulation of nerves and tissues (De Domenico 1982; Nikolova 1987;

Low & Reed 1990), which might result in the physiologic effects of IFC. Some current evidence (Palmer *et al.* 1999, 2004; Johnson & Tabasam 1999b, Kinnunen & Alasaarela 2005), suggests that the modification of the AMF parameter has a marginal effect on the activation of physiologic responses. Moreover, investigations into the effects of different "beat" frequencies of IFC on experimentally induced pain have found that the analgesia was not influenced by the "beat" frequency when IFC was applied at strong but comfortable intensity without muscle contractions (Johnson & Tabasam 1999a b, 2003a b; Noble 2000). This new evidence is relevant since the selection of AMF has conventionally been the central parameter of clinical decision making with IFC.

Despite the profuse use of IFC in clinical practice, its effectiveness is controversial. The findings of some controlled trials using experimental pain models provides evidence to support the rationale for using IFC (Stephenson & Johnson 1995; Tabasam & Johnson 1999 ; Johnson & Tabasan 1999a, 2002, 2003a b; Cheing & Hui-Chan 2003; Shanaham *et al.* 2006; McManus *et al.* 2006),while others question its efficacy (Alves-Guerreiro *et al.* 2001, Minder *et al.* 2002; Stephenson & Walker 2003).

Pressure algometry is the most common modality used to apply a uniform rate of pressure for inducing experimental mechanical pain. The pressure pain threshold (PPT) is defined as the minimum pressure (mechanical stimulus) that induces pain (Ogimoto *et al.* 2002). The algometry and the assessment of PPTs have been widely and successfully used in various trials in order to assess treatment results (Alves-Guerreiro *et al.* 2001; Farasyn & Meeusen 2003, 2005 ; Aspegren *et al.* 2003; Chesterton *et al.* 2003; Ylinen *et al.* 2003; McManus *et al.* 2006).

The contradictory findings concerning the clinical effectiveness of IFC make increasing the scientific evidence for the analgesic effect of IFC based on controlled conditions imperative. It is equally important to evaluate the influence of the AMF parameter on the physiologic and therapeutic effects of IFC in order to guide clinicians in decision-making with interferential current therapy.

The purpose of this study was to investigate the hypoalgesic effect of interferential current therapy on an experimental mechanical-induced pain model in normal subjects receiving two different interferential current treatment protocols.

In addition, the evaluation of the role of the AMF component in the PPT outcome and the PPT gender differences in the response to the IFC protocols was considered.

1.2 DEFINITION OF TERMS

Mechanical experimental pain model: The mechanical pain model includes the application of a mechanical stimulus that evokes pain. The stimulus that produces the sensation is known and also controlled by the investigator under laboratory conditions. This control includes the nature, localization, frequency, intensity and duration of the mechanical stimulus (Staahl & Mohr 2004). Among the various noxious stimuli, pressure-induced pain models are believed to assess deep tissue reflecting its sensitivity to pain (Kosek *et al.* 1999; Prushansky *et al.* 2004).

Algometry: Pressure algometry is the most common modality used to apply a uniform rate of pressure to induce mechanical pain and for quantitative analysis of muscle pain

and tenderness. Pressure algometry is a safe technique that includes the evaluation of both the pressure pain and tolerance thresholds (Handwerker & Kobal 1993).

Algometer: The pressure algometer or 'pressure threshold meter' is a manual instrument (e.g. mechanical or electronic) that, when pressed against the body surface, measures pressure (Jensen 1990). It is also designed to quantify and record levels of tenderness via a pressure threshold measurement. The algometer is a force gauge fitted by a rubber disk with a surface of 1 cm^2 (Fisher A. 1987a). It may indicate pressure in different units (e.g. kilograms, pounds, or newtons per unit area), and knowing the size of the contact area allows the values to be transformed into the appropriate pressure units (e.g. kilopascals, newtons per square centimeter, or kilograms per square centimeter) (Jensen 1990).

Pressure Pain Threshold: The pressure pain threshold (PPT) is defined as the minimum pressure (stimulus) necessary to evoke a first sensation of pain (Ogimoto *et al.* 2002) or as the amount of force required eliciting a sensation of pain distinct from pressure or discomfort (Fisher 1987a, 1998). PPT is generally used to assess the sensitivity of the nervous system to noxious stimuli. PPT measurements using a pressure algometer are used for the evaluation and follow-up of various pain syndromes (Prushansky *et al.* 2004).

Interferential current: The interferential current (IFC) is a medium frequency current based on the physical phenomenon of wave interference (Kloth 1991). The interferential current is produced by mixing two medium frequency currents that are slightly out-of-

phase in the range of 4000-5000 Hz (Palmer & Martin 2002). The currents are delivered by two separate pairs of electrodes through separate channels within the same machine. These electrode pairs are configured against the skin so that the circuits cross and the currents produce an interference pattern (Figure 1). One of the circuits is always introduced at a constant frequency, e.g. 4.000 Hz, while the frequency of the second one is variable, e.g. between 4000-4100.

Amplitude modulated frequency (AMF) or beat frequency: The difference between the frequencies in circuits 1 and 2 (Kloth 1992). When two currents of 4000 and 4100 Hz are mixed, an AMF of 100 Hz results (Nikolova 1987). The beat frequency applied to excitable tissues is perceived as rhythmical sensory or motor pulsations, or both, depending on the maximum amplitude of the beat modulation (Kloth 1991).

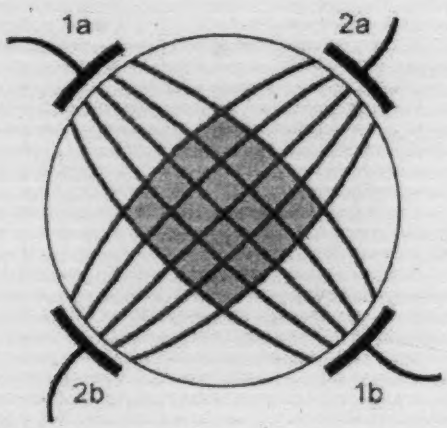


Fig.1 The interference pattern produced by the interaction of two IFC circuits. From: Ozcan J., Ward AR., Robertson VJ. (2004). A Comparison of True and Pemodulated Interferential Currents. *Arch Phys Med Rehabil* 85 : 410.

1.3 OBJECTIVES OF THE STUDY

The objectives of this study were as follows:

1. To investigate the hypoalgesic effects of interferential current therapy on an experimental mechanically-induced pain model in normal subjects.

a) To describe the hypoalgesic effect of interferential current therapy on pressure pain threshold using an amplitude-modulated frequency (AMF) parameter of 100 Hz and the effect of interferential current therapy without using the amplitude-modulated frequency (AMF = 0 Hz) parameter in healthy males and females.

b) To compare the hypoalgesic effect of interferential current therapy on pressure pain threshold using an amplitude- modulated frequency (AMF) parameter of 100 Hz and the effect of interferential current therapy without the use of an amplitude-modulated frequency parameter (AMF = 0 Hz) in healthy males and females.

1.4 RESEARCH HYPOTHESES

The following hypotheses were investigated in this study:

1. Interferential current therapy will increase the pressure pain threshold during and after the application of the treatment protocols in the study group.
2. The frequency of the amplitude modulated (AMF) parameter will not influence the increase of the pressure pain threshold in the subjects in the study group.

1.5 LIMITATIONS OF THE STUDY

This study was limited by:

a) The ability of researcher to apply the same procedure for every subject. The possible confounders to be controlled were:

   i) IFC electrode placement: the reference for placement electrodes was the same for every subject (lumbar area).

   ii) Measurement bias was controlled by the use of a valid and reliable test instrument (algometer).

   iii) The evaluator was trained in the use of the algometer until consistent measurements were achieved (i.e. the reliability of measurements falls within the range of ICC 0.75- 0.80), about one month prior to beginning the experimental procedure.

   iv) The instrument and the area of application were the same for all subjects (landmarking will be used to allow easy recognition of the point of the algometer application).

   v) The instrument was calibrated every week for the duration of the experimental procedure in order to ensure that the same rate force (1 $kg/cm^2/seg$) being applied is consistent.

   vi) The same evaluator was blinded for the assessment of all subjects.

   vii) The instructions were the same for every subject and were based on an instruction sheet.

   viii) Placebo effect. Since IFC machines are technically impressive, a potential placebo effect could appear. This factor was controlled by the

IFT units being hidden from the subjects' view during the experimental procedure.

b) The ability to generalize the results because of the use of a convenience sample.

1.6 DELIMITATIONS OF THE STUDY

This study was delimited to:

1) Healthy subjects
2) An experimental mechanical-induced pain model

1.7 ETHICAL CONSIDERATIONS

This investigation was performed maintaining total privacy and confidentiality of the subjects. All procedures (assessment and treatment) were non-invasive and there was no potential risk with the application of algometer or the interferential current treatment. The project was approved by the HREB Ethics Committee of The University of Alberta and informed consent from the subjects was obtained before the individuals were enrolled in the study. The benefits of this study were to provide a better basis and understanding to physical therapists who work to control the pain of their patients.

CHAPTER 2: LITERATURE REVIEW

2.1 HUMAN EXPERIMENTAL PAIN MODELS

Pain research in humans can investigate simpler types of pain, such as that induced under controlled conditions by precisely calibrated noxious stimulus of different sensory modalities and of varying intensities (Crawford 2001). Under experimental pain conditions, individuals participate voluntarily, and can be used as their own control, thereby minimizing inter-individual response variation, and variation over time (Arendt-Nielsen & Sumikura 2002). Also, using healthy subjects, in the absence of any pathophysiological process or potentially interacting medications, allows optimal conditions for answering basic scientific questions related with the use of analgesics (Fillingim 2002).

In experimental pain methods, the stimulus that produces the sensation is known and is controlled by the investigator under laboratory conditions. This control includes the nature, localization, frequency, intensity and duration of the stimulus (Staahl & Mohr 2004). These parameters of the stimulus can be defined and kept constant and the physiological and psychophysical responses can be quantified (Arendt-Nielsen & Sumikura 2002). Thus, a subject's responses can be attributed to the experimental manipulation. Similarly, such pain-inducing methods should not produce any tissue damage, psychological injury or any other health hazard to the subject, and should have no after-effects following termination of the experiment (Wolff 1984).

Experimental pain (e.g. cold, ischemic, heat, mechanical) is often induced in a standardized way to assess the effectiveness of treatment modalities in healthy subjects. Furthermore, as healthy subjects are relatively homogeneous within a group, the different responses of different groups may be explained by group allocation rather than by variations in individuals. In contrast, patients suffering from clinical pain tend to have variations in terms of history, severity, or cause of pain. Consequently, it is difficult to form homogeneous groups at the baseline (Cheing & Hui-Chan 2003).

Muscle pain can be induced experimentally by a variety of methods. Pain arising from muscle without involvement of external stimuli is termed an "endogenous pain model". Ischemic and exercise induced-muscle pain are typical endogenous models. Conversely, the activation of peripheral nociceptors by external stimuli (e.g. mechanical, electrical or chemical) is considered as the application of "exogenous modalities" (Svensson & Arendt-Nielsen 1995). Regardless the method used, a basic tenant of experimental pain is the presence of a stimulus to evoke pain and the ability to measure the response to the painful stimulus (Arendt-Nielsen & Sumikura 2002). In addition, some authors (McCain 1987; Gracely 1994; Le Bars *et al.* 2001; Dionne *et al.* 2001), state that an experimental pain stimulus, used in an experimental pain model, should include the following essentials:

- Be non invasive, and produce no irreversible tissue damage.
- Be specific, measuring pain and no other sensations.
- Be sensitive, being able to measure pain within a range that is ethically acceptable and physiologically relevant.
- Be measurable, and show a relationship between stimulus and pain intensity.

- Be variable, from zero to maximal tolerable levels.
- Be repeatable, with no change in the response over time.
- Be sensitive enough to measure the effect of the analgesic agent.

The ultimate goal of advanced human experimental pain research is to obtain a better understanding of mechanisms involved in pain transduction, transmission, and perception under normal and pathophysiologic conditions (Arendt-Nielsen & Svensson 2001).

2.2 MECHANICAL STIMULATION AS EXPERIMENTAL MODEL OF PAIN (ALGOMETRY)

Using a mechanical stimulus is a typical exogenous experimental model. Among the various noxious stimuli, pressure-induced pain models are believed to assess deep tissue reflecting its sensitivity to pain (Kosek *et al.* 1999; Prushansky *et al.* 2004). Reliability of muscle tenderness can be improved if, instead of using the finger to apply pressure, the examiner uses an instrument that applies a constant pressure over a specific anatomical point (Farella *et al.* 2000).

Pressure algometry is the most common modality used to apply a uniform rate of pressure for inducing mechanic pain and for quantitative analysis of muscle pain and tenderness. The tenderness or pressure pain sensitivity is expressed quantitatively by the pressure pain threshold (PPT), or the minimum pressure that induces pain or discomfort (Fisher 1987a, 1998). Thus, by using this model, both pressure pain threshold and tolerance thresholds can easily be measured (Fisher 1998; Staahl & Mohr 2004).

Moreover, the use of algometry to measure the pressure pain threshold has been shown to be valid and convenient method of monitoring treatment effects (Harris & Rollman 1983; Nussbaum & Downes 1998; Potter *et al.* 2006).

Pressure algometry is the most frequently applied technique for clinical pain testing (Handwerker & Kobal 1993). In addition, the algometry and the assessment of PPTs have been widely and successfully used in various trials in order to assess treatment results in patients (Côte *et al.* 1994; Pratzel 1998; Hsieh *et al.* 2002; Farasyn & Meeusen 2003, 2005; Ylinen *et al.* 2003) and individuals without pain (Walsh *et al.* 1998; Alves-Guerreiro *et al.* 2001; Aspegren *et al.* 2003; Chesterton *et al.* 2002, 2003a; MacManus *et al.* 2006) to assess the hypoalgesic effects of physical therapy treatments. An advantage of pressure algometry in the management of pain is that it facilitates communication among clinicians and researchers and allows quantitative comparison of their findings (Fisher 1997).

The use of pain-free healthy subjects will make an objective evaluation of the magnitude of the PPT for a controlled noxious stimulus possible. Such data are difficult to obtain in clinical settings where the stimulus that elicits pain in patients may be of uncertain origin (Johnson & Tabasan 2003a). Despite the good correlation between induced changes in PPT by pain treatments and changes in the clinical status of pain, the use of healthy subjects can limit the generalizability of the results.

Despite the several advantages of pressure algometry, its limitations should be kept in mind. When using a mechanical stimulation model, the skin is inevitably stimulated, thus confounding the influence of skin and muscle pain on sensory and motor responses (Svensson & Arendt-Nielsen 1995). Hence, the model is non- specific. Several

studies attempted to eliminate the contribution of skin sensation by using a local anesthetic cream before assessing the pressure pain sensitivity (Graven Nielsen *et al.* 1998; Kosek & Ekholm 1995; Kosek *et al.* 1999; Laursen *et al.* 1997). The results of these studies showed either decreased or unchanged pressure pain sensitivity after the anesthetic cream application. The authors also concluded that tissue sensitivity assessed by pressure was a combination of cutaneous and deep tissue mechanosensitivity. However, group III (thin myelinated) and IV (non-myelinated) afferent fibers from deep tissue would be strongly involved in the sensation evoked by algometry (Graven-Nielsen 2006).

In addition, algometry is based on the subjective response of the patient, therefore the results can be manipulated (Fischer 1998). Other concerns regarding pressure algometry are related to its capacity to maintain a constant compression rate and the physical effort needed in multiple measurements (Polianskis *et al.* 2002).

The literature suggests that there are sexual differences in the experience of PPTs. However, the results are controversial. For example, it has been proposed that women have lower PPTs than men (Fisher 1987a, Brennum *et al.* 1989; Hogeweg *et al.* 1992; Vanderweën *et al.* 1996; Rollman & Lauterbacher 2001; Chesterton *et al.* 2003b). Hormonal variables have been used to explain this assumption. Iseelee *et al.* (2001) have documented the menstrual cycle effect on human pain perception. They showed that PPTs of masseter, temporalis and thumb muscles were significantly lower during perimenstrual phases in women using and not using oral contraceptives. Similarly, during the follicular phase, PPTs are, in general, significantly lower (Bajaj *et al.* 2001).

However, other authors reported no gender differences in PPT (Vatine *et al.* 1993; Hogeweg *et al.* 1996; Farasyn & Meeusen 2002; Christidis *et al.* 2005).

Despite the question regarding the size of this difference and the clinical relevance of this difference, it is clear that woman and men differ in their perception to experimental pain, with woman exhibiting a comparatively great sensitivity (Riley *et al.* 1998).

Based on their good inter-rater and intra-rater reliability and validity, algometric measurements have been extensively used as both a clinical (Vanderweën *et al.* 1996; Farella *et al.* 2000; Maquet *et al.* 2004; Ylinen *et al.* 2005, 2006) and as an exogenous experimental pain model (Walsh *et al.* 1998; Alves-Guerreiro *et al.* 2001; Chesterton *et al.* 2002, 2003a; Prushansky *et al.* 2004; Christidis *et al.* 2005) to assess tissue sensitivity and to evaluate the efficacy of therapeutic modalities in patients as well as normal subjects. Treatment-induced changes in PPT observed in laboratory settings are believed to correlate well with changes in the clinical status of pain, and as such, PPT is considered a useful experimental model (Fisher 1987b). Because algometry can provide a quantitative measure of such change, and as soft tissue tenderness may change with treatment, PPT measurements are commonly used for the evaluation and follow-up of various myofascial pain syndromes (Prushansky *et al.* 2004).

2.3 THE ALGOMETER

The pressure algometry technique uses an instrument called an algometer. The algometer is a pressure gauge attached to a rod that registers the force expressed in

pressure units such as kilograms per square centimeter per second ($Kg/Cm^2/s$), Newtons per square centimeter per second ($N/Cm^2/s$), or kilopascals per second (kPa/s). Since the recently available algometers are calibrated more conveniently in kilograms, the data are often presented in metric units (Fisher 1987a). Despite the pressure units used, a higher reading indicates lower pain sensitivity or higher pain threshold. The force is perpendicularly (Figure 2) applied to the tissues via a small ($1cm^2$) rubber footplate, to mimic human fingertip area performing a manual localized pressure palpation (Nussbaum & Downes, 1998; Prushansky *et al.* 2004). During the procedure of assessing PPT, subjects are instructed to differentiate the pressure from a feeling of "being pressed" to "initial pain recognition (threshold)" (Ogimoto *et al.* 2002). When the change in sensation occurs, the pressure exerted moves an indicator in a clockwise direction and the instrument is immediately removed to read the pressure threshold. Pressing the zeroing button returns the indicator to zero after each measurement (Vanderweën *et al.* 1996).The force recorded is the amount of pressure that evokes pain (PPT). The sensation of pressure and pain is the result of stimulation of nerve endings in superficial as well as deeper tissues (Jensen 1990).

Fig. 2 Algometric technique using a mechanical type algometer on the back area. The rod of the algometer is maintained perpendicular to the surface of the measured muscle. The right hand grasping the gauge prevents deviations from the perpendicular angle while increasing the pressure at a steady rate.

From a functional and construction perspective, two categories of algometers are commonly used in the pressure algometry technique:

1. Mechanical analog devices (Figure3) consist in a handheld instrument with an indicator that moves in a clockwise direction, continuously indicating the applied pressure.
2. Digital electronic devices (Figure 4), which is a more sophisticated instrument and includes a built-up transducer, electronic recording and digital display unit.

Moreover, there is a subject-activated push button connected via cable to the instrument to release the pressure at the first feeling of pain.

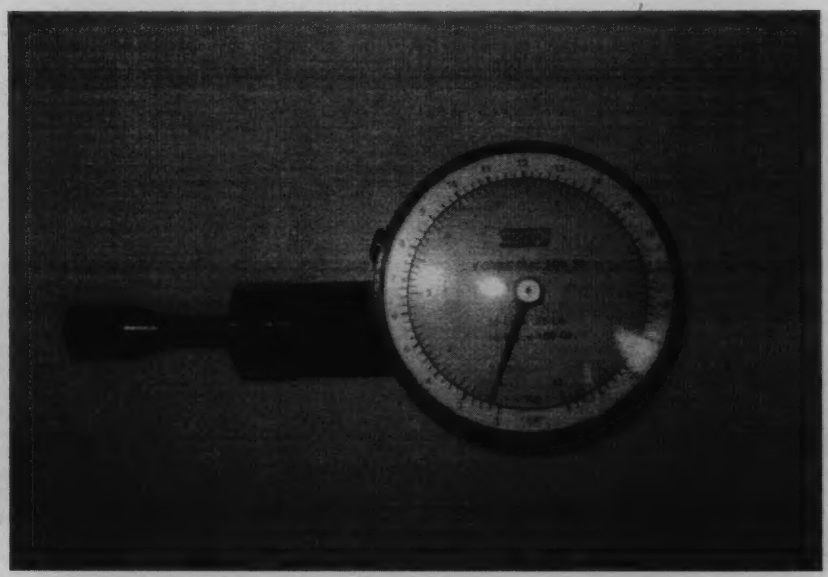


Fig. 3 Mechanical algometer

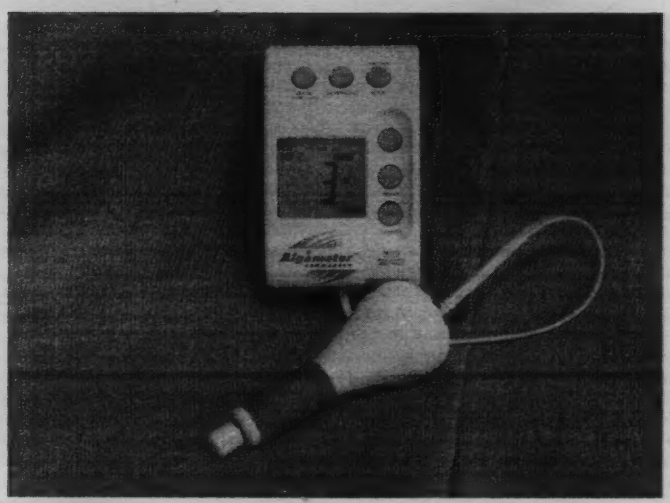


Fig.4 Electronic algometer http://healthsciences.qmuc.uk/labweb/Equipment/Algometer.htm.

With the mechanical algometer, when the PPT is reached, the instrument is immediately removed to read the pressure threshold. With the electronic algometer, the reaction time of the examiner is eliminated because on reaching the pain threshold, the subject is the one who activates a button to release the pressure. It has also been reported that the use of electronic devices may reduce the variation in the rate of pressure increase (Ohrbach & Gale 1989). These authors also stated that electronic tools provide examiners with visual cues to improve their timing. In the same way, some studies conclude that reliability is enhanced when PPT measurements are taken by electronic algometer (Brennum *et al.* 1989; Vatine *et al.* 1993; Kosek *et al.* 1993). However, it has been showed that intra-examiner reliability with non- electric algometry appears to be as good (ICC range 0.75- 0.89) as the electrical type in healthy subjects (Antonaci *et al.* 1998; Nussbaum & Downes 1998).

The mechanical analog algometer allows the examiner to continuously monitor the pressure increments, maintained at a constant rate (i.e. 1 kg/sec). Such monitoring is difficult with digital devices because the numbers change too fast to be read, thus the pressure can not be increased properly (Fischer 1998). Another advantage of the mechanical devices is that they are pocket size so they can be carried along with other diagnostic instruments. It has been proposed that sophisticated and expensive electronic devices provide little additional advantages when compared with analog mechanical. As a result, the mechanical analog algometer should be preferred (Fischer 1998).

The importance of increasing pressure at a standardized rate has been emphasized based on findings that higher PPT scores were recorded at higher application rates (List *et al.* 1991). The rates suggested are between 0.5 $Kg/Cm^2/s$ (Kosek *et al.* 1999; Chesterton

et al. 2003a; Christidis *et al.* 2005) and 1 $Kg/Cm^2/s$ (Vanderweën *et al.* 1996; Farasyn & Meeusen 2003, 2005; Hastie *et al.* 2005; Ylinen *et al.* 2005). Similarly, the algometry technique habitually includes consecutive instead of single PPT measurements (Ogimoto *et al.* 2002; Farasyn & Meeusen 2003; Prushansky *et al.* 2004; Christidis *et al.* 2005 ; Hastie *et al.* 2005; Chesterton *et al.* 2005; Jason *et al.* 2005). It has been reported that use of the mean of several measurements provides a more reliable estimate of PPT when compared with a measurement alone (Naussbaum & Downes 1998).

The time interval between PPT measurements varies from 5 seconds (Ohrbarch & Gale 1989) to 10 minutes (Chesterton *et al.* 2003a). The use of repetitive application of noxious stimuli with a short time interval between can decrease the pain threshold (sensitization of nociceptors) (Prushansky *et al.* 2004). In addition, it has been proven that lowered threshold on the second consecutive measurement is the result of a possible local irritation (Kosek *et al.* 1993). Conversely, long stimulus intervals can decrease the subject's ability to focus on a specific site inducing an elevation of the thresholds (Prushansky *et al.* 2004). Thus, pain threshold measurements require a reasonable inter stimulus interval not only to eliminate possible sensitization but also to maintain the subject's and examiner's alertness. In this regard, studies have shown no significant changes in PPT in the course of repetitive measurements using either 10 sec or 20 sec intervals (Merskey & Spear 1964; Jensen *et al.* 1986; Brennum *et al.* 1989; Naussbaum & Downes 1998; Faranasyn & Meeusen 2003; Prushansky *et al.* 2004; Hastie *et al.* 2005).

It has been shown that pressure pain sensitivity is larger in areas having nerve trunks (muscle/nerve sites) in comparison to pure muscle sites (Kosek *et al.* 1999). Measurements of PPT over "bony" and "pure" muscle points using handheld algometry

do not differ however (Kosek *et al.* 1999; Polianskis *et al.* 2001). In other words, PPT at muscle sites can be the same or higher than at "bony" sites. Normal values for various muscles have been established (Fisher 1987a) (Table 2.1).

Table 2.1 Pressure threshold in normal persons. From: Fisher AA. (1987a). Pressure algometry over normal muscles. Standard values, validity and reproducibility of pressure threshold. *Pain* 30:115-126.

PRESSURE THRESHOLD IN NORMAL PERSONS (kg/cm^2)

Muscle	Females		Males		Difference between males and females
	Mean	S.D.	Mean	S.D.	
Upper trapezius	3.7	1.9	5.4	2.8	2.5 *
Pectoralis major	–	–	5.4	2.4	
Levator scapulae	4.6	1.9	5.6	2.2	2.2 *
Teres major	4.2	1.5	6.4	2.3	3.9 **
Supraspinatus	4.6	2.2	6.7	3.0	2.8 **
Gluteus medius	6.5	2.8	6.8	2.7	0.5^{NS}
Infraspinatus	5.4	2.8	7.3	2.8	2.4 *
Middle deltoid	5.1	2.3	7.7	2.7	3.6 **
Paraspinals L 2 cm	6.1	2.4	8.8	2.4	3.9 **
Paraspinals L 4 cm	6.8	3.0	9.0	2.7	2.6 *

$$\text{Force in kg} = \frac{\text{Newton} \times 0.102 \text{ kg}}{\text{Newton}}$$

* $P < 0.05$.

** $P < 0.01$.

2.4 RELIABILITY OF ALGOMETRIC MEASUREMENTS

Because of their constant area of stimulation and the control over the rate and direction of pressure application, algometers are highly reliable (List *et al.* 1991; Farella *et al.* 2000; Potter *et al.* 2006). There is growing evidence regarding the support of PPT reproducibility and validity when measured with a pressure algometry. Thus, in several studies, algometric measurements have been shown to have good or excellent inter-rater values ranging from ICC 0.74 to 0.90 (Orbach *et al.* 1998; Nussbaum & Downes 1998)

and intra-rater reliability values ranging from ICC 0.75 to 0.99 (Brennum *et al.* 1989; Orbach *et al.* 1989; 1998; Farasyn & Meeusen 2003; Prushansky *et al.* 2005; Ylinen *et al.* 2005, 2006; Potter *et al.* 2006; Cathcart & Pritchard 2006). In addition, Antonaci *et al.* (1998) found an ICC 0.84 for intra-examiner reproducibility in healthy subjects as well as an ICC 0.75 for the inter-examiner reliability. Despite a great inter-individual variation in the PPT, Ogimoto *et al.* (2002) found significant intra-individual correlations ($r = 0.8$) and validity among the measurement sites in the oral mucosa. In the same way, Farella *et al.* (2000), pointed out that pressure algometry might reach acceptable values of sensitivity (0.77) and specificity (0.87) for the temporalis muscle when used in the diagnosis of myofascial pain of the jaw muscles. Prushansky *et al.* (2004), reported good to excellent reproducibility (ICC 0.85-0.96) in two protocols of cervical PPT measurements in healthy subjects. Finally, Fisher (1987a), in a study concerning the pressure algometry in normal muscles, provided evidence regarding the excellent reproducibility and validity of pressure threshold measurement.

2.5 INTERFERENTIAL CURRENT

Interferential current therapy (IFC) was developed in the 1950s by Dr. Hans Nemec in Austria. IFC was also first described in the English-language literature by its inventor, and appears to be more published information on IFC than any of the other TENS-like device (Johnson 2001) except TENS itself. The term interferential therapy stems from the idea of two currents "interfering" which each other and this gives rise to the term "interferential therapy" or less used "interference therapy". The interferential

current may be described as the transcutaneous application of alternating medium-frequency electrical currents, amplitude modulated at low frequency for therapeutic purposes (Palmer & Martin 2002). Nemec´s description of IFC includes two fundamental aspects. First, by using medium frequency alternating currents, skin impedance is minimized. Second, if two medium frequency alternating currents are applied to the body simultaneously, they will produce a low-frequency "beating" effect (Nemec 1959).

The IFC uses two out-of-phase circuits in the range of 4000-5000 Hz. One of the circuits is always introduced at a constant frequency, e.g. 4.000 Hz, while the frequency of the second one is variable, e.g. between 4000-4100 (Figure 5). Thus, the difference between two currents is from 0 to 100 Hz (Nikolova 1987).

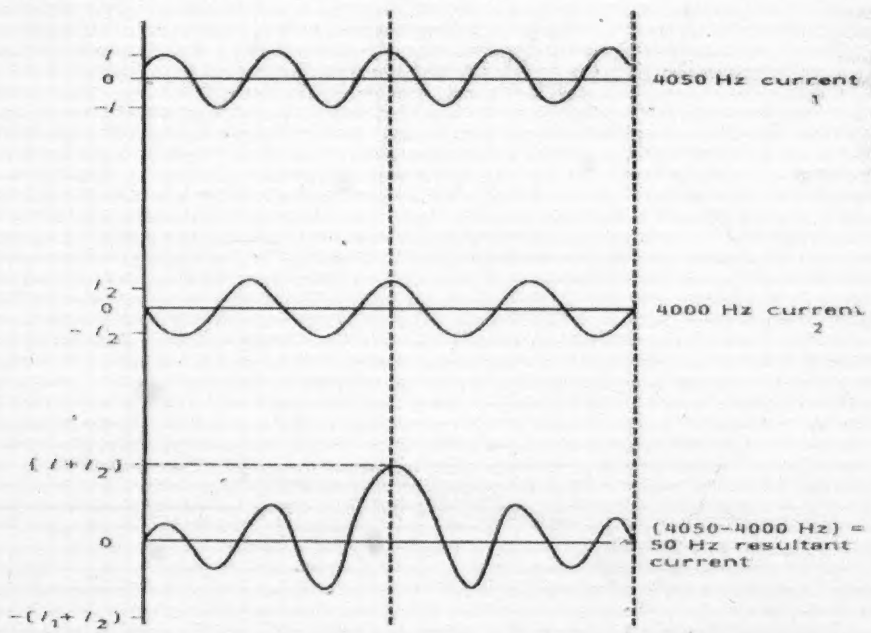


Fig. 5 Alternating medium frequency currents (4050 Hz, 4000Hz), amplitude modulated at low frequency (50 Hz). From: Goats C.G. (1990). Interferential current therapy. *Br. J. Sp. Med* 24 (2): 87.

IFC stimulators are designed to generate an amplitude-modulated interference wave that rhythmically increases and decreases in amplitude at low frequency. The rate at which the amplitude of the resultant current rises and falls is equal to the difference in frequency present between the two original currents (Figure 6). This new low frequency current is commonly called an amplitude-modulated frequency (AMF) or beat frequency (De domenico 1982: Nikolova 1987; Goats 1990; Mehreteab 1993; Palmer & Martin 2002).The results of questionnaire surveys in England (Pope *et al.* 1995), Canada (Lindsay *et al.* 1995), and Australia (Lindsay *et al.* 1990; Robertson & Spurritt 1998) have shown that IFC is widely used throughout the world. In addition, these studies illustrate both a high rate of access to IFC stimulators and a high rate of usage as well.

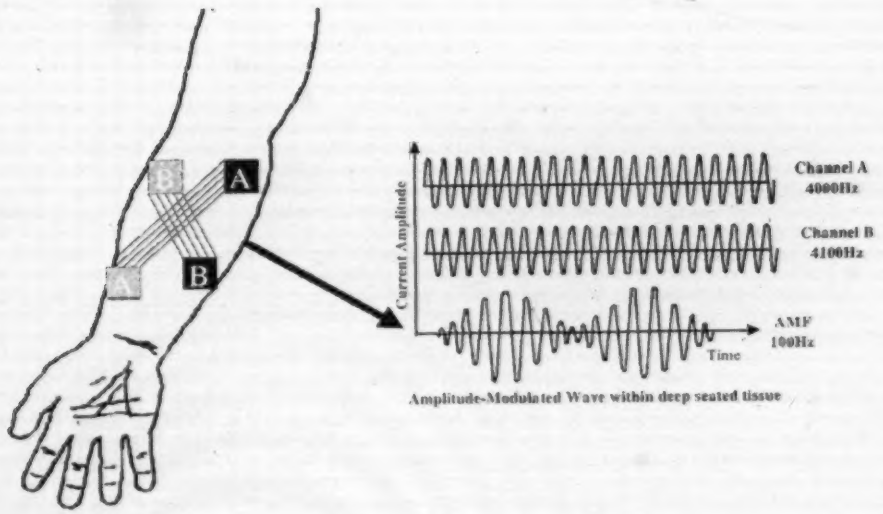


Fig. 6 Principles used to generate amplitude – modulated interference wave within deep tissue. From: Johnson, MI. (2001). Transcutaneous Electrical Nerve Stimulation (TENS) and TENS-like devices: do they provide pain relief? *Pain Reviews* (8): 135.

2.5.1 PROPERTIES OF INTERFERENTIAL CURRENT

The electrical properties of tissue provide the reason for introducing medium frequency alternating current into clinical practice (Ward & Robertson 1998). In agreement with the Nemec´s IFC statements, the skin acts a capacitive barrier to the flow of current. As the frequency of the applied current increases, the skin offers progressively lower impedance (Low & Reed 1990). Thus, the advantage of medium frequency currents (i.e. IFC) is based on their capacity to diminish the impedance offered by the skin and subcutaneous tissues, which is a problem for low frequency currents (i.e. TENS), while still producing low frequency effects within the tissues (Low & Reed 2000). By diminishing the skin resistance, the discomfort normally incurred by traditional low-frequency currents is also reduced (Palmer & Martin 2002). According to this theoretical explanation, the medium frequency current serves as a carrier current to easily pass the skin impedance and then operates as low amplitude modulated frequency (AMF) in the tissues. With medium-frequency currents, a higher proportion of electrical energy is available to stimulate tissue under the superficial epidermis (Meyer-Waarden et al. 1980; Ward & Robertson 1998). Interferential current therapy exploits the principle of interference to maximize the current permeating the tissues whilst reducing to a minimum unwanted stimulation of cutaneous nerves. Thus, the purpose of IFC would appear to be to deliver currents to deep-seated structures (Goats 1990; Johnson 2001; Palmer & Martin 2002).

2.5.2 AMPLITUDE MODULATED FREQUENCY (AMF) PARAMETER

AMF or "beat" frequency is the result of the interaction of two out of phase medium frequency circuits (Figure 7). For instance, if the first circuit has a constant frequency of 4000 Hz and the second one of 4100, then the result is a new low frequency current (AMF) with a beat frequency of 100 Hz. It is theorized that the medium frequency component simply act as a "carrier" current, bringing the low frequency AMF into the tissues, where the body must be able to modulate it (De domenico 1982).

The AMF has been traditionally considered to be the effective component of IFT (De domenico 1982; Nikolova 1987; Low & Reed 2000). Some authors have referred the AMF as the "biological frequency range" responsible of therapeutic effects (De domenico 1982) However, recent evidence in healthy subjects questions this belief (Johnson 1999; Palmer *et al.* 1999, 2004; Johnson & Tabasam 2003a; Kinnunen & Alasaarela 2005). A modification of AMF has been shown to have little effect on the threshold activation of sensory (Kinnunen & Alasaarela 2005), motor and pain responses (Palmer *et al.* 1999; Johnson & Tabasam 2003a). These observations suggest that the AMF does not mimic low frequency stimulation. Moreover, a 0 AMF (pure 4000 Hz current) showed similar effects on nerve excitation when an AMF was used (Palmer *et al.* 1999). Thus, it has been theorized that the medium frequency component of IFC (i.e. 4000 Hz) would be the dominant stimulation parameter (Palmer *et al.* 1999; Johnson 2001; Palmer & Martin 2002).

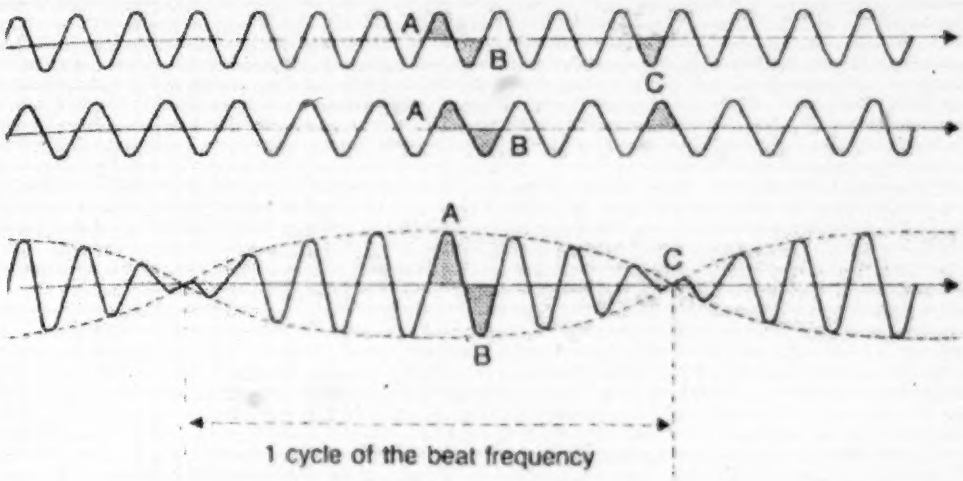


Fig. 7 AMF. At certain points, the two phases of the circuits will match identically (A&B) the resultant will produce an overall increase in amplitude. At other points (C) are equal and opposite, thus cancelling each other out. The dotted line shows the shape of the AMF frequency cycle. The number of these "beats' per second represent the AMF of the current. From: De domenico G. (1982). Pain relief with interferential therapy. *The Australian Journal of Physiotherapy* 28 (3): 17.

The selection of the AMF has been believed to play an important role in the physiological effects and the therapeutic responses, creating a differential stimulation of nerve and tissues (Wodsworth & Chanmugam 1983; Nikolova, 1987; Goats 1990; Low & Reed 1990, 2000). The mechanisms by which this occurs is still obscure (Johnson 1999). Although, empirical evidence fails to support this classical theory, it has been cited that by selecting different AMF settings, IFC would produce beneficial treatment outcomes in a number of clinical conditions such as musculoskeletal and vascular conditions, urogenital dysfunction and pain (De domenico 1982; Savage 1984; Nikolova 1987; Goats 1990) . Even though, evidence supporting the use of IFC on the control of edema appears anecdotal, some indications have been described. For example, an AMF of 100 has been

recommended for the reduction of acute edema (Goats 1990), while chronic edema can be treated using a two-stage application. Initially an AMF 100 Hz to promote vasodilatation followed by an AMF 10 Hz to activate musculoskeletal pump. In contrast, recent evidence concluded that IFC failed in reducing the edema experimentally induced by either formalin or carrageenan (Jorge *et al.* 2006).

More specifically, for pain control, texts recommend AMF settings of 80-130 Hz (Table 2.2) (De domenico 1982; Savage 1984; Goats 1990; Kloth 1992; Watson 2000, 2002) for activating pain gating mechanisms. Also, AMF settings of 25 Hz and lower (De domenico 1982; Goats 1990; Watson 2000, 2002) would stimulate the descending pain suppression mechanisms. However, it is still not known whether the amplitude modulated wave (AMF) of IFC can selectively stimulate different populations of nerve fibers (Johnson 1999).

In summary, claims that the active component of IFC is the AMF, and that different AMF settings are responsible for a variety of physiological and therapeutics effects, especially in pain control, is currently a matter of controversy and needs to be confirmed.

Table 2.2 Proposed hypoalgesic mechanisms and suggested AMF settings

Hypoalgesic mechanism	Suggested AMF setting
Pain Gate/ sensory fibre stimulation	80-100 Hz (De domenico,1982) 90- 100 Hz (Savage,1984) 100 Hz (Goats, 1990) 80- 130 Hz (Watson 2000, 2002)
Descending pain supression/nociceptive fiber stimulation	10- 25 Hz (De domenico, 1982) 15 Hz (Goats, 1990) < 10Hz (Watson 2000,2002)
Placebo	Not specifically implicated

2.5.3 INTERFERENTIAL THERAPY TECHNIQUES

Based on the number and disposition of electrodes used, IFC can be therapeutically applied by using two techniques; the quadripolar method and the bipolar method.

2.5.3.1 QUADRIPOLAR TECHNIQUE

In a quadripolar electrode arrangement, know as true IFC, the medium frequency alternating carrier currents are applied at the skin surface via two isolated circuits. Therefore, the four electrodes are applied to the body in a "clover-leaf" pattern to allow mixing (interference) of the two currents and formation of the endogenous amplitude-modulated beats. This produces maximum interference within the central portion of the electrical field, with less interference beneath the electrodes (Wodsworth & Chanmugam 1983; Kloth 1991; Low & Reed 1990; Selkowitz 1999). Some sources claim that this technique gives good deep efficiency and comfort to patients (Low & Reed 1990; Goats 1990; Kloth 1991).

The "clover- leaf" pattern depicted in textbooks, however, seems to be merely theoretical. This has been only reproduced in a homogeneous medium (water) (Treffene 1983). In biological tissues (i.e. pork), the pattern is unreliable and uneven (Demmink 1995).

The electrodes may be applied cross-diagonally to the body in either a planar (Figure 8) arrangement (all electrodes on one surface), or a co-planar (Figure 9)

(electrodes on opposing surfaces) (Kloth 1991). The leads are color-coded to ensure correct arrangement of the circuits (Low & Reed 2000).

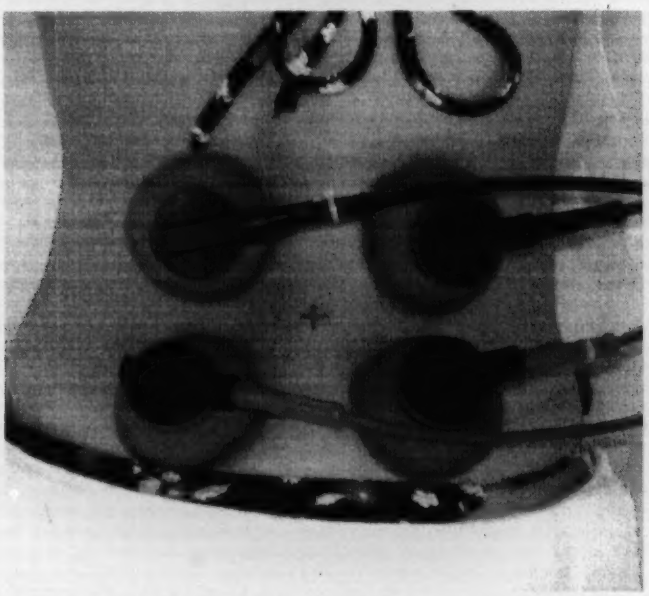


Fig. 8 Quadripolar planar electrode application technique

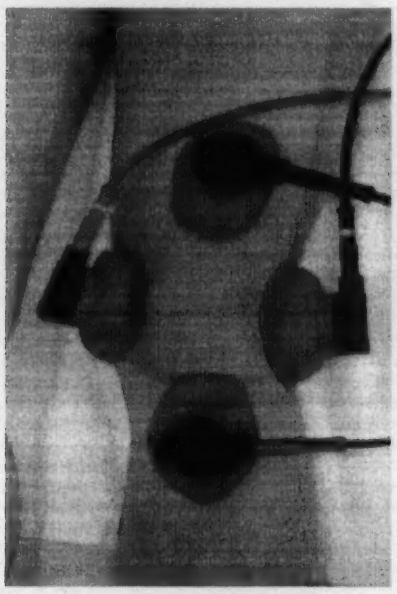


Fig. 9 Quadripolar co-planar electrode application technique.

2.5.3.2 PREMODULATED OR BIPOLAR TECHNIQUE

The bipolar method is an alternative method for delivering IFC from the two circuits exogenously within the device and delivers the premixed amplitude-and frequency-modulated beats (AMF) via two electrodes (Figure 10) (one circuit) to the patient's skin (Kloth 1991). In other words, the currents are mixed in the stimulator prior to its application via two electrodes (Palmer & Martin 2002). With this technique, the beats are pre (amplitude) modulated within the device and are delivered directly to the skin. The bipolar method does not provide endogenously formed IFC beats because the two alternating currents are mixed inside the device (Kloth 1991). Moreover, it has been shown that by using the bipolar method, the maximal current intensities are accumulated under the electrodes. The intensity of the current decreases as it goes into deeper tissues (Hansjuergens 1986). However, recent evidence (Ozcan et al. 2004) questions this belief. They reported that premodulated IFC is clinically more effective than true IFC in terms of deep efficiency. Thus, more research is needed to determine the superiority of one delivery method (i.e. quadripolar, bipolar) over another.

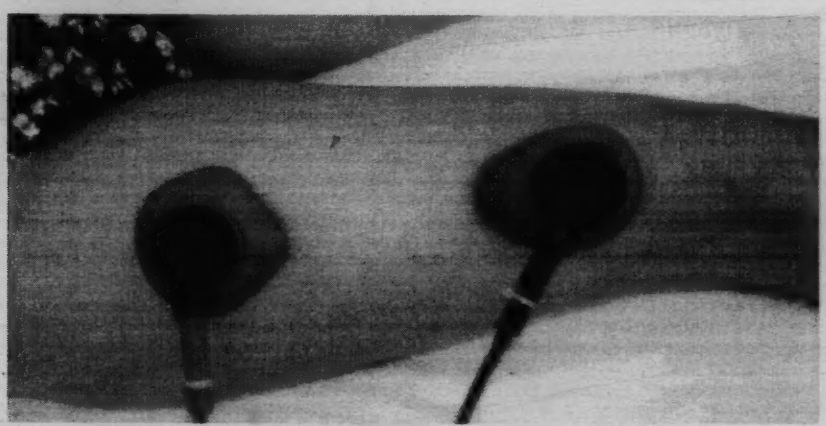


Fig. 10 Bipolar application technique for premodulated IFC via two pad electrodes

2.5.4 TYPE OF ELECTRODES AND ELECTRODE PLACEMENT

Interferential therapy is applied either via flat carbon rubber electrodes or via electrodes that are held in an area using an intermittent suction unit (vacuum electrodes). The carbon rubber electrodes (Figure 11) may be used with water-soaked sponges or gel and are secured by rubber straps or bandages (Low & Reed 1990). The vacuum electrodes use a suction unit connected to the interferential equipment. With this modality, metal electrodes mounted inside flexible rubber cups (Figure 12) are connected by wires to a pump that can provide a negative pressure (Low & Reed 1990; 2000). It is inadvisable to use suction on skin of poor quality that may break down; for example, in severe edema or in the elderly (Low & Reed 2000). The use of suction (vacuum) electrodes does not appear to provide any additional therapeutic benefit beyond that of the modality itself, although they are easier to apply, especially to the large flat areas such as the low back, shoulder and hip (Savage 1984; Watson 2000). In contrast, flat carbon rubber electrodes may be easier to apply to peripheral limbs, when held in position by bandages or elastic straps (Palmer & Martin 2002).

With regards to electrode placement, when applying interferential current, most clinicians place the electrodes in a way that currents cross one another in the target tissue (Wodsworth & Chanmugam 1983; Nikolova 1987; Low & Reed 1990, 2000; Kloth 1991; Watson 2000), although in the case of pain management, placing the electrodes over the spinal nerve root, nerve trunk, or appropriate dermatomes can also be considered (Nikolova 1987; Watson 2000).

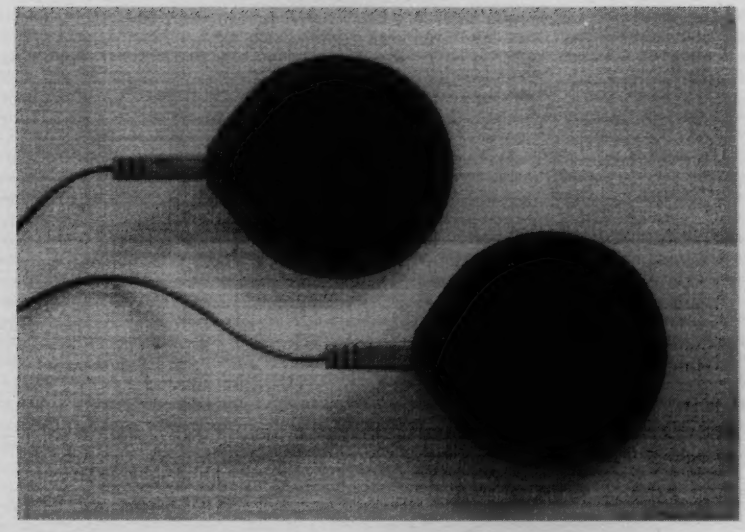


Fig. 11 IFC Rubber electrodes

Fig. 12 IFC vacuum electrodes. The metal electrodes are mounted inside flexible rubber cups with sponges pad to maintain optimum conductivity.

2.5.5 IFC CURRENT INTENSITY

The current level is adapted to suit the subjective sensitivity of the patient. There is a general consensus among the literature (Wodsworth and Chanmugan 1983; Nikolova 1987; Johnson 2001), and for clinical (Taylor et *al.* 1987; Hurley et *al.* 2001; Jarit *et al.* 2003), and experimental trials (Minder *et al.* 2002; Johnson & Tabasam 2002, 2003a b; Stephenson & Walker 2003; Palmer *et al.* 2004) that the current dosage should produce a "strong but comfortable sensation" at the site of the pain when used for pain relief. This level of intensity is obtained by slowly increasing current amplitude so that the subject reports either that the current level is uncomfortable or that the motor threshold has been reached (determined by the experimenter observing visible muscle contractions) (Johnson & Tabasam 2003a b; Palmer & Martin 2002). In addition, periodic adjustments of the intensity are advisable to compensate for the adaptation phenomena (Wodsworth and Chanmugan 1983; Savage 1984; Goats 1990). However, recently, Defrin *et al.* 2005 demonstrated that it is not necessary to adjust current intensity during treatment to obtain pain relief in osteoarthritis pain. They suggest that despite apparent A-fiber adaptation, peripheral nerves are still sufficiently activated to induce analgesic effects.

2.5.6 IFC TREATMENT DURATION

Despite the fact that some authors claim that the analgesia produced by stimulation of IFT may be induced within 15 minutes (Kloth 1992; Cheing & Hui-Chan 2003) , treatment time constraints in the clinical setting varies between 10-20 minutes

(Savage 1984; Wodsworth and Chanmugam 1983) with a maximum of 30 minutes (Nikolova 1987). However, when investigating IFT effects in an experimental setting, most researchers use a treatment time ranging between 20- 30 minutes (Johnson & Tabasam 2002, 2003a b; Minder *et al.* 2002; Jarit *et al.* 2003; Cheing & Hui-Chan 2003). It should be pointed out that these clinically used treatment durations have an unclear theoretical basis that is supposed to be based on practical constraints rather than scientific rationale (Johnson 1999). Also, in the experimental environment, the use of longer treatment times may be related to controlled conditions present under laboratory conditions.

With regards to the post-stimulation effect of interferential currents, there is some evidence, in experimentally induced cold pain, that the IFT has short-lasting effects with cold pain threshold returning to baseline levels within 10-20 minutes post-stimulation (Johnson & Wilson 1997; Johnson & Tabasam 1999a). In other words, the greatest effect of IFC would occur mainly during its application rather than after treatment has ended. However, Cheing & Hui-Chan (2003), in an experimental heat pain model, demonstrated that 30 minutes of IFT significantly elevated the heat pain threshold during the stimulation, and the analgesic effect lasted at least 30 minutes after the stimulation. The results of these studies and the lack of investigation of this issue in clinical scenarios continue to stimulate debate regarding the post treatment effects of IFT.

2.5.7 IFC PRECAUTIONS AND CONTRAINDICATIONS

Although contraindications are based on prudence as opposed to scientific evidence, it is inadvisable to use interferential current therapy in the following conditions (Wodsworth & Chanmugam 1983; Nikolova 1987; Kloth 1991; Watson 2000; Palmer & Martin 2002):

- Where disturbance of a thrombus, spread or infection or cancerous cells, or hemorrhage might result.
- With patients who do not comprehend the clinician's instructions or who are unable to co-operate.
- Patients with pacemakers.
- Severe hypertension or hypotension.
- Dermatological conditions (e.g. eczema, dermatitis).
- Where elevated body temperature or a disease process increases local cellular metabolism.
- Where the application of electrodes over the anterior aspect of the neck and carotid sinus is required.
- Where the application of electrodes is over the abdomen during pregnancy.
- Where the application of electrodes is over the eyes.
- Where the application of electrodes is over the chest wall in patients with cardiac problems.

2.5.8 ANALGESICS MECHANISMS OF INTERFERENTIAL CURRENT THERAPY

One of the most common clinical uses of IFC is for the treatment of pain by electroanalgesia (Kloth 1991). Several theoretical physiological mechanisms associated with the analgesic effect of IFC such as the "gate control" theory, increased circulation, descending pain suppression, physiological block of nerve conduction and placebo have been claimed to support its analgesic effect (De domenico 1982; Goats 1990; Palmer & Martin 2002).

- The pain gate theory. The "pain gate" theory suggests that impulses in large diameter sensory nerves (Aβ fibers) inhibit dorsal horn neurons normally responsive to nociceptive afferent nerves (C and A δ fibers) (Melzack & Wall 1965). IFC is capable of stimulating large diameter peripheral nerve fibers (Aβ), which may reduce the output of the transmission cells, thus reducing the perception of pain. The use of frequencies around 100 Hz are thought to be responsible for these effects (Wodsworth & Chanmugam 1983; Savage 1984; Low & Reed 1990, 2000; Kloth 1992; Watson 2000, 2002). Moreover, pulse duration stimulus of approximately 100 to 200 microseconds is believed to be able to selectively activate the large diameter afferent fibers (De domenico 1982).
- Increased circulation. A local increased fluid flow and fluid exchange as a consequence of mild muscle contraction may help to remove chemical irritants affecting pain nerve endings and reduce local tissue pressure (De domenico 1982; Wodsworth & Chanmugam 1983; Goats 1990; Low & Reed 1990). Savage (1984) suggested the activation of IFC over sympathetic nerves at 0-5 Hz as a possible

mechanism for increasing fluid flow. However, more recent studies have found no evidence of increased tissue perfusion with IFC stimulation (Nussbaum *et.* al 1990; Indergand & Morgan 1995). Another study showed that the significant increase in the blood flow was no greater than placebo IFC (Olson *et. al* 1999).

- Descending pain suppression. This mechanism may be mediated by the activation of A δ and C fibers leading to the release of inhibitory neurotransmitters (e.g. encephalin and endorphin) at the spinal level (De domenico 1982; Low & Reed 1990; Goats 1990). This mechanism is probably activated by IFC at lower frequencies of 10-25 Hz (De domenico 1982; Low & Reed 1990) or in the 2-5 Hz range (Watson 2002).
- Physiological block of nerve conduction. Stimulation of peripheral nociceptive fibers at rates above their maximum conduction frequency may cause cessation of action potential propagation (Low & Reed 1990; Goats 1990). For example, the C fibers fire at frequencies below 15 Hz. When the frequency of stimulation increases, the conduction in the C fibers decreases (Cheing & Hui-Chan 2003). It has been proposed that IFC, using frequencies above 50 Hz, may lead to temporary physiological block of finely myelinated and non-myelinated nociceptive fibers (Low & Reed 1990). However, authors also stated that a physiological block of nerve fibers have not been demonstrated with IFC stimulation (De domenico 1982; Ganne 1986)
- Placebo. Since interferential machines are impressive, a placebo effect with IFC treatments may be expected (Low & Reed 1990). Taylor *et al.* (1987) studied the analgesic component of IFC in patients with recurrent jaw pain. They showed no statistically difference between treatment and placebo groups. Conversely, a couple of studies (Adedoyin *et al.* 2002; Defrin *et al.*2005) assessed the effects of IFC on

osteoarthritis pain. They found that IFC applied to the knee significantly reduced pain intensity when compared to the placebo group. However, the extent of placebo responses with IFC stimulation remains unclear (Palmer & Martin 2002).

Although several theoretical physiological mechanisms have been proposed in the literature to support the analgesic effects of IFC, conclusive evidence is still elusive (Palmer & Martin 2002). Moreover, the lack of published clinical studies using a patient control and objective methods of assessing pain suppression produced by IFC treatment cannot support the claims made in the textbooks (Kloth 1991; Johnson 1999,2001; Palmer & Martin 2002).

2.5.9 EFFECTS OF IFC IN CLINICAL TRIALS

Medium frequency currents are mainly used for sensory and motor stimulation (Ward & Robertson, 1998). The sensory effects of IFC on clinical pain have been broadly investigated, including trials on osteoarthritis pain (Quirk *et al.* 1985; Ni Chiosoig *et al.* 1994; Adedoyin *et al.* 2002; Defrin *et al.* 2005; Adeyoyin *et al.* 2005a), chronic jaw pain (Taylor *et al.* 1987), ankle (Christie & Willouhby 1990) and humerus (Martin & Palmer 2000) pain fractures, low back pain (Checchia 1991; Werners *et al.* 1999; Hurley *et al.* 2001, 2004; Adedoyin *et al.* 2005b), lumbosacral radiculopathy (Al Abdulwahab & Beatti 2006), fibromyalgia (Almeida *et al.* 2003; Raimundo *et al.* 2004), soft tissue shoulder disorders (van der Heijden *et al.* 1999) and postoperative knee pain (Jarit *et al.* 2003). However, despite the widespread areas where the effects of IFC have been studied,

systematic research regarding the analgesic effect of IFC under strictly controlled conditions are still limited (Johnson & Tabasam 2002).

The results of the clinical application of IFC on acute and chronic pain tend to be positive in terms of support its analgesic effectiveness, applied alone or as part of a multimodal treatment plan. However, these results must be interpreted with caution because of the poor quality of the studies (Fuentes *et al.* 2006).

2.5.9.1 EFFECTIVENESS OF IFC ON CHRONIC PAIN

The effectiveness of IFC on chronic pain has been extensively studied using the knee osteoarthritis pain model. For example, in a randomized, single blind, placebo controlled design, Adedoyin *et al.* (2002), allocated 30 patients alternatively into IFC or placebo groups. The treatment group received a total of eight 20-minute 80-100 Hz IFC treatment sessions over four weeks. Pain ratings in the IFC group were found to be significantly better than that for the placebo group. However, this study did not include random sample selection, the randomization procedure was not described, included a small sample size (30) along with a low power (0.26), and had no description of validity and reliability of the outcomes. In other study, Adedoyin *et al.* (2005a), showed an effective analgesic profile when using IFC , but this study did not include a control/placebo group, making it difficult to conclude whether patient improvement was a result of the active treatment or not.

The effects of IFC on osteoarthritis pain were also investigated by Defrin *et al.* (2005). In this trial, 62 patients were randomly assigned into 4 active, placebo and control groups. Real and sham treatments included 12 IFC (30-60 Hz) sessions, 20 minutes per session for 4 weeks. The outcome measurements included chronic pain

intensity (VAS), morning stiffness, and ROM among others. After completing the treatment, the IFC applied to the knee significantly reduced both chronic pain intensity and stiffness and significantly increased pain-free ROM in the knee when compared with placebo group. Despite the inclusion of both placebo and control groups in its design, this study's sample selection was not randomized and there was no description of the validity or reliability of the measurements. In addition to the small statistical power calculated (0.20), the randomization procedure was not described and information regarding dropouts was not included.

In the same way, Quirk *et al.* (1985), in a pilot study, compared the effects of IFC, shortwave diathermy, and exercises in the treatment of osteoarthrosis of the knee. They showed a significant improvement in the mean pain scores and clinical condition after the application of different therapeutic modalities. However, the results of this study cannot be totally supported because of its small sample size (n= 38) and power (0.21), the absence of a blinded component and most importantly, no inclusion of a control/placebo group. Atamaz *et al.* (2006) and Ni Chiosoig *et al.* (1994) reached similar favorable effects using IFTC in osteoarthritis pain. Nevertheless, the results of these studies cannot be interpreted as clinically significant because the very low power (0.38 and 0.15 respectively). Equally important, the results of these studies may have been influenced by other factors involved in the application of treatments since they did not include a control/placebo group to isolate the modality effects.

In shoulder pain disorders, Van der Heijden *et al.* (1999), in a randomized, double blind, placebo controlled trial reported the effect of IFC plus ultrasound (US) on the effect of exercise for shoulder pain disorders. They randomized 180 patients into one of

the following groups in addition to exercises: 1) active 60-100 Hz bipolar IFC plus US; 2) active 60-100 Hz bipolar IFC plus dummy US; 3) dummy IFC plus active US; 4) a placebo group consisting of dummy IFC plus dummy US; and 5) exercise only. The main outcome measures included recovery, shoulder disability questionnaire (SQD), pain (VAS) and ROM at six weeks after the treatment had been completed and at intervals up to one year. Because most patients in all treatment groups improved without having significant differences in outcomes between the groups at all time intervals, the authors concluded that neither IFC nor US were effective as adjunctive to exercise therapy for soft tissue shoulder disorders.

2.5.9.2 EFFECTIVENESS OF IFC ON ACUTE PAIN

The analysis of the effectiveness of interferential current therapy applied for acute pain is far less profuse than for chronic pain. Studies have focused on acute low back pain and knee surgery pain conditions. An overall analysis of these trials suggests that IFC may be helpful when treating acute painful conditions. Nevertheless, as well as in chronic pain, the findings must be interpreted with caution because of methodological shortcomings shown in the trials.

Hurley *et al.* (2001), report no differences in improvements for pain or disability among two groups of IFC with different electrode arrangement. One group included electrodes in the painful area plus "The Back Book". The second group's electrodes were applied over the nerve root plus "The Back Book". The control group included only "The Back Book". Methodological shortcomings included the low power of the study (0.34) and the poor control of confounders. Also, since all groups received "The Back Book", it is difficult to conclude from this study that IFC is an effective modality for reducing pain

in acute low back pain. Recently, Hurley *et al.* (2004) assessed the difference in short and long-term effectiveness of IFC and manipulative therapy in acute low back pain. They concluded that there was no difference in pain and disability benefits between the groups. Despite the good power reported (0.90), the main limitations were that therapists were not blinded to the content of each protocol, and the absence of control group. In this regard, the observed improvements could merely reflect the effect of natural history of the acute pain, and regression to the mean of being simply a placebo.

Finally, Jarit *et al.* (2003) reported the favorable effects of IFC on pain, edema, ROM, and analgesic medication consumption when compared to placebo in knee surgery pain. Although the results suggest that IFC may be helpful in post-operative recovery from knee surgery, there are several methodological flaws that can contrast the conclusions of this study. Firstly, the very low power (0.18) reported. Secondly, the lack of appropriate control of the confounders. Thirdly, the fact that a non-blinded company representative participated in the study and instructed active and placebo patients on use of the IFC units may have introduce bias. Fourth, there was no description of a randomization procedure. Fifth, the study showed lack of information regarding the validity and reliability of outcome measurements. Finally, the statistical analysis used was not appropriate and may have overestimated some of the differences reported in the study.

2.6 EFFECTS OF IFC ON EXPERIMENTAL PAIN TRIALS

Contrary to clinical studies, conditions during experimental trials are more controlled. In experimental pain methods, the stimulus that produces the sensation is known and also controlled by the investigator. In the clinical setting, there is minimal experimental control over the painful stimulus, which can contribute to increased variability in patient responses (Fillingim 2002).

Several recent trials using experimentally induced pain were performed in an attempt to evaluate the effectiveness of IFC. Most of the studies about the effect of IFC on laboratory pain conditions have been conducted using the cold-pressor pain model (Stephenson & Johnson 1995; Johnson & Wilson 1997; Tabasam & Johnson 1999; Johnson & Tabasam 1999a b, 2003a, 2003b; Stephenson & Walker 2003; McManus *et al.*2006; Shanahan *et al.* 2006). The immersion of the hand in iced water (cold-pressor) has been shown to be a popular and reliable method for inducing pain. However, its application is limited, due that only distal segments can be immersed.

On the other hand, few other studies have been carried out in other experimental pain conditions. For example, two investigations (Schmitz *et al.* 1997rm; Minder *et al.* 2002) intended to assess the hypoalgesic effectiveness of IFC using the eccentric exercise pain model. This model is related to induce delayed onset muscle pain (DOMS). Similarly, little information exists regarding the hypoalgesic effects of IFC in the mechanically induced pain model. In this regard, only two studies (Alves-Guerreiro *et al.* 2001; McManus *et al.* 2006) have been conducted. The mechanical pain was identified as a less uncomfortable method for pain induction than the cold model (McManus *et al.*

2006). Due its versatility and safety, the pressure algometry has been used in all type of structures and zones, including bony and muscle points assessed in upper extremities, lower extremities, cervical and lumbar spine, and face muscles. The information about the effects of IFC on ischemic pain is also limited, with only two investigations having been conducted (Scott & Purves 1991; Johnson & Tabasam 2002)

Finally, less studied, the heat (Cheing & Hui-Chan 2003), and the chemically induced inflammatory pain model (Jorge *et al.* 2006) have been also incorporated as experimental modalities for assessing the hypoalgesic efficiency of IFC.

The results of these trials suggest that experimentally induced pain is influenced by IFC. The hypoalgesic effects of IFC appear to be mainly associated with an increase in pain thresholds rather a change in pain tolerance, unpleasantness or pain intensity outcomes (VAS).

The hypoalgesic effects of IFC appear to be more consistent in some pain models than others. For example, a succession of studies using the cold-pressor pain model demonstrated, in a reliable manner, an increase in cold pain threshold while applying IFC (Stephenson & Johnson 1995; Johnson & Wilson 1997; Johnson & Tabasam 1999a; Tabasam & Johnson 1999; Shanahan et al. 2006; McManus et al. 2006). However, using a similar methodology, other authors evaluated the analgesic effects of IFC in experimentally cold-pressor pain in healthy subjects, finding that IFC did not significantly alter the pain threshold (Stephenson & Walker 2003).

In other models, such as the eccentric exercise, ischemic, and mechanical models, the evidence of the hypoalgesic influence of IFC produced conflicting results. For example, Alves-Guerreiro *et al.* (2001), using mechanically-induced pain, found no

significant differences in the mechanical pain threshold. They concluded that IFC (150 Hz) did not produce a significant hypoalgesic effect. Conversely, McManus *et al.* (2006) found that the application of IFC (100Hz) significantly increased the mechanical pain threshold during the treatment compared with baseline. The same pattern was found in the eccentric exercise pain model with both positive and negative effects being reported. For example, Schmitz *et al.* (1997) evaluated the effects of IFC at high (100 Hz) and low (10 Hz) beat frequencies on experimentally-induced DOMS. Results revealed a significant change in perceived pain scores. Conversely, Minder *et al.* (2002) using the same IFC parameters (10-20 Hz; 80-100Hz), found no overall beneficial effect on pain intensity for delayed onset muscle soreness compared to controls or a placebo. Finally, Scott & Purves (1991) examined the effects of IFC on ischemic pain induced by the tourniquet test in 15 healthy volunteers. They concluded that IFC did not elevate time to tolerance of ischemic pain when compared to a sham application. Conversely, Johnson & Tabasam (2002), showed that IFC significantly reduced pain intensity when compared to sham and control groups.

The selection of the optimal stimulation parameters for IFC has been a controversial and unclear topic. For some authors (Wodsworth & Chanmugam 1983; Nikolova 1987; Savage 1992), frequencies of 100 Hz are in the analgesic and sedative range. However, there is no evidence supporting such a claim (Johnson 2001). Moreover, with experimentally pain, when using different frequency patterns (e.g. 10-30, 80-100 Hz), the effect of IFC was not affected by the frequency pattern used (Minder *et al.* 2002; Stephenson & Walker 2003).

Often, the selection of the parameters of stimulation is based on personal clinical experiences rather than being founded on empirical evidence. Most commonly, the main criterion for choice appears to be the patient's report of his/her comfort with the stimulation (Johnson & Tabasam 2003a).

In spite of limited empirical evidence existing to support it, the literature cites the AMF parameter as the most effective component of IFC (Wodsworth & Chanmugam 1983; Kloth 1992; Low & Reed 1990, 2000; Goats 1990; Savage 1991). It is believed that AMF stimulates the nerves and tissues (De domenico 1982; Nikolova 1987; Low & Reed 1990, 2000), resulting in a physiologic mechanism that leads to pain relief. However, based on current evidence, this paradigm is changing. For example, Johnson & Tabasan (1999b, 2003a) failed to find any difference in the magnitude of the elevation on cold pain threshold or pain ratings across a range of AMF (20, 60, 100, 140, 180, and 220) of IFC in healthy subjects. They stated that experimental cold pain was not influenced by AMF frequencies. Most relevant, Palmer *et al.* (1999), concluded that the medium frequency component of IFC was the main parameter of stimulation based on the fact that a pure 4 kHz IFC current (AMF=0) did not produce different effects on nerve excitation from those produced when AMF was included. Recently, Palmer *et al.* (2004) found that an AMF setting of 0 Hz (pure 4 kHz current) was no less effective in the alteration of C and delta fiber-mediated thermal threshold than was an AMF of 5 Hz or 100 Hz. In the same way, Kinnunen & Alasaarela (2004) investigated the sensory thresholds at different AMF settings (10Hz, 30Hz, 50Hz, and 100Hz). Because the sensory thresholds were unaffected for the different frequencies among healthy volunteers, they conclude that AMF had a minor role in sensory threshold values.

Most of the recent evidence questions the importance of the AMF component in the therapeutic effects of IFC and at the same time, suggests that the medium frequency component (4000 Hz) could be the main element to evoke stimulating effects.

Despite several studies that have been carried out (De domenico 1982; Quirk 1985; Nikolova 1987; Young *et al.* 1991; Werners *et al.* 1999; Martin *et al.* 2000; Hurley *et al.* 2001; Jarit *et al.* 2003), there have been few attempts to investigate, systematically, the sole analgesic effect of IFC under strictly controlled conditions. Similarly, no study has compared the influence of the AMF= 0 in the analgesic response of IFC on mechanically- induced pain, using algometry.

The aims of this study were to contribute the scientific research based in controlled conditions in order to assess the analgesic effect of IFC on mechanical induced pain in healthy subjects as well as to evaluate the influence of AMF component of IFC.

CHAPTER THREE: METHODS AND PROCEDURES

3.1 SUBJECTS

A convenience sample of 46 healthy subjects aged between 18 and 40 years old was recruited for this study. The sample included 23 female and 23 males (α =0.05, β = 0.20, power = 80%, and effect size 0.25 (Stevens 2002)). Subjects were continually recruited until 46 subjects were found.

3.2. INCLUSION CRITERIA

To be included in this study, the subjects had to:

1. be males or females between 18 – 40 years old. This age group was selected because it includes an adult population for which pressure pain thresholds (PPTs) standard values have been documented (Table 2.1) (Fisher 1987a).

2. be healthy subjects with no acute or chronic pain or clinical pathology, especially relatedto the lumbar spine. Subjects must not have suffered from neurological problems (central or peripherical) that could interfere with the experimental procedure and the outcomes.

3. be subjects taking no medication especially affecting the musculoskeletal system such as anti-inflammatory or pain relief drugs, muscle relaxants or arthritic medications.

3.3 EXCLUSION CRITERIA

Subjects were excluded from this study if they had:

1. Any contraindications to the use of electrotherapy (see Appendix 2).
2. Any acute or chronic clinically – painful condition
3. Taking analgesic or anti-inflammatory medication.

3.4 SUBJECT RECRUITMENT

Subjects for this study were recruited from students, staff or people who attend the University of Alberta or living in the surrounding areas, using advertising in the Faculties of Engineering, Education, the University of Alberta International Student Network (UAIS), and the Students' Union Building (see Appendix 1).

All subjects were given an inform consent to read, all questions regarding the study were answered, and they signed the informed consent to be part in the study, in accordance with University of Alberta's policies on research using human subjects (see Appendix 3)

3.5 STUDY DESIGN

This study was a randomized cross-over design using one group as its own control (repeated measures design). The subjects were blinded to the interferential current therapy treatment protocols (AMF=100 Hz; AMF= 0 Hz). In addition, in order to avoid

the potential biasing effect of the protocol treatment sequence, the order of treatment was randomized by simple randomization (i.e. "throwing a dice"). Similarly, to keep potential rater bias to a minimum, an assistant was the responsible for applying the IFC protocol. Moreover, the investigator in charge of measuring PPTs was blinded to the type of IFC protocol applied to the subjects. Also, this investigator was blinded to the statistical analysis of data.

Interferential current therapy makes it possible to assess the pressure pain threshold before, during, and after the procedure using each subject as his/her own control. Since each subject is exposed and measured on each response measure, much of the variability that exists between different subjects is automatically reduced. Thus the sensitivity of the experiment is increased. Additionally, this design facilitated the comparison among measurements because the information came from the same individual (helping make groups equivalent). Under this design, an individual's characteristics were stable (e.g. gender, age). Thus, any differences observed among the treatment conditions could be attributed solely to the treatment (Gross & Watkins 2000). Finally, it has been suggested that the algometry reliability is improved where each individual serves as his/her own control (Fisher 1987a, Merskey & Spear 1964), and when the technique is conducted by the same investigator (Woolf 1979).

3.6 DATA COLLECTION: EXPERIMENTAL PROCEDURE SEQUENCE

3.6.1 DEMOGRAPHIC DATA COLLECTION

Demographic data were collected for all subjects who met the inclusion criteria to help better characterize the sample being examined. These data included age, gender, weight and height. The gender variable was used in a posteriori analysis to determine whether that factor have an effect on PPT.

3.6.2 EQUIPMENT

Two electrical stimulation treatment protocols were applied using interferential current therapy equipment (Intellect Legend Stim Chattanooga Group Inc.), (see Appendix 5 for specifications). The interferential current therapy equipment (Figure 13) met safety standards (see Appendix 6). The equipment was calibrated to make certain the parameters of stimulation remain constant for the study.

3.6.3 INSTRUMENT

The modification of painful threshold was registered using a mechanical algometer. The algometer registered the force expressed in kg/cm^2 which gave an objective way

(metric units) of measuring the pain threshold in the subjects. The algometer was calibrated (Appendix 7) and applied using a constant rate pressure force of 1 kg/cm^2/seg (Farasyn & Meeusen 2003, 2005; Hastie *et al.* 2005; Ylinen *et al.* 2005).

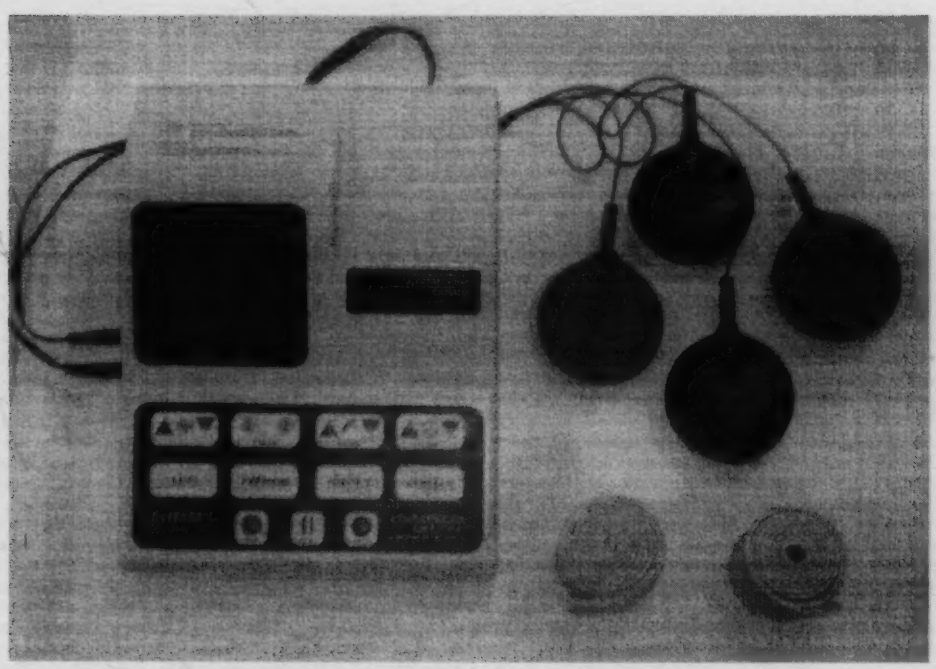


Fig. 13 Interferential therapy current equipment

3.6.4. PROCEDURE AND TESTING ENVIRONMENT

The intervention in the study considered the application of two randomly assigned interferential current therapy (IFC) protocols. The difference between the two protocols was based on two different parameters of stimulation. The first protocol included a 100Hz AMF component while the second included a 0 Hz AMF parameter. Both protocols used a quadripolar planar technique with carbon rubber electrodes placed over the lumbar area of the subjects (see Appendix 8). In the same way, the current intensity for both treatment protocols was a strong but comfortable sensory level "pins and needles-like sensation." without visible twitches (Nikolova 1987; Johnson 2001; Hurley et *al.* 2001; Minder *et al.* 2002; Johnson & Tabasam 2002, 2003a b; Jarit *et al.* 2003; Palmer *et al.* 2004).

The experimental procedure involved two visits for applying the two protocols for each subject. To avoid a temporary or permanent change in pain variable resulting from the first treatment (carryover effect), the first and second treatment protocols were applied with at least a minimum of 1 day rest between them (washout period) (Eble *et al.* 2000; Cheing & Hui-Chan 2003; Johnson & Tabasan 2003a). The experimental procedure was first explained through the use of a standard information sheet, after which any issues were clarified (see Appendix 9) before testing began at the first attendance.

During the first visit, the following procedure was conducted:

1. Subjects' personals and demographic data were recorded. In addition, the information letter and consent form were given to the subject.
2. Normal skin sensation was established at the stimulation site (lumbar area) using hot and cold-water filled test-tubes and blunt pinprick.

3. Subjects were instructed in the application of the algometer (previously calibrated (Appendix 7), given a demonstration and then underwent a practice test of PPT measurements using the dominant forearm until the subject felt that he/she understood the sensation and what he/she was being asked to do.
4. A short IFC stimulation was performed on the non dominant forearm of the subject, as a practice trial, in order to ensure a correct identification of the stimuli applied, and also to familiarize the subject with the level of electrical stimulus required for the experimental procedure.
5. The randomization of treatment protocol order (100 Hz AMF or 0 Hz AMF) was chosen by the "throwing a dice" method.
6. The subject was lying in a prone position with the arms relaxed alongside the trunk.
7. The subject received, using the quadripolar planar IFC technique, either 100 Hz AMF parameter or 0 Hz AMF (according to the randomization order) for 30 minutes over the lumbar area.
8. A mechanical algometer, at a constant rate pressure force of 1 $kg/cm^2/seg$, was applied to register the values of pressure pain threshold (PPT) before, during and after the application of the IFC protocol previously randomized. The experimental procedure (Figure 14) included the collection of the mean of three consecutive (20 seconds in between) measurements of PPT for each subject:

   a) Three measurements of PPT were collected 10 minutes prior to the treatment in order to acquire baseline values. The mean of these measurements was used as the pretest value (M1).

b) Three measurements of PPT were collected right before initiating IFC treatment. The mean of these measurements was used as a test value (M2).

c) Three measurements of PPT were collected 15 minutes into IFC treatment. The mean of these measurements was used as a test value (M3).

d) Three measurements of PPT were collected immediately IFC treatment had stopped (30 min). The mean of these measurements was used as a test value (M4).

c) In order to assess the post stimulation analgesic effects of IFC on PPT values, three measurements of PPT were collected 30 minutes post treatment. The mean of these measurements was used as a test value (M5).

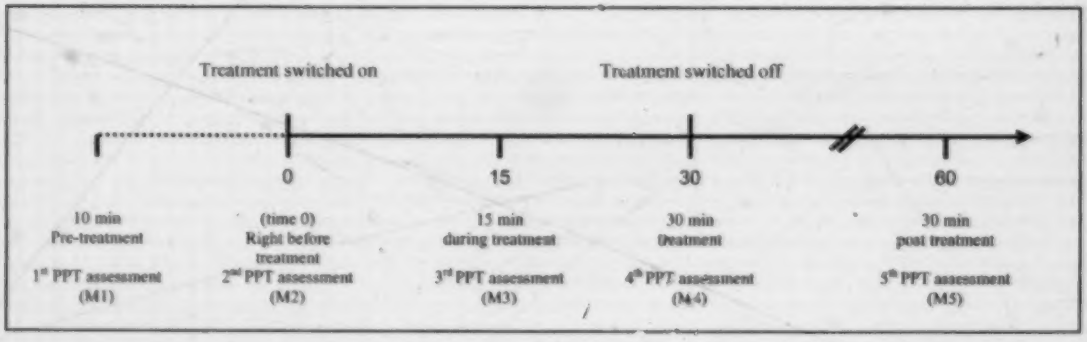


Fig. 14 The experimental procedure. Description of the recordings of Pressure Pain Thresholds at different time intervals during the study.

The mechanical algometer was applied perpendicularly, using a small ($1cm^2$) rubber footplate, over the right erector spinae muscle, 4 cm to the right of the spinous process of L4 (Figure 15). The lower back muscles area was chosen because it has been used in clinical (Farasyn & Meeusen 2005; Jason *et al.* 2003), and experimental settings

(Fisher 1987a; Farasyn & Meeusen 2003), and good to excellent intra-examiner reliability has been reported (Fisher 1987a; Farasyn & Meeusen 2003, Orbach 1989), and normative values are available (Fisher 1987a).

Fig.15 Mechanical algometer applied perpendicularly using a small ($1Cm^2$) rubber footplate over the right erector spinae muscle, 4 cm to the right of the spinous process of L4.

In order to ensure reproducibility, a landmark was considered at the anatomic point described above. The force recorded by the algometer was the amount of pressure that evoked the first sensation pain (pressure pain threshold). For this reason, the subjects were asked to say "stop" as soon as they felt a clear sensation of pain, distinct from pressure or discomfort.

At the second attendance, the following procedure was followed:

1. Normal skin sensation was established again at the stimulation site (lumbar area) using) using hot and cold-water filled test-tubes and blunt pinprick.
2. The subject was lying in a prone position with the arms relaxed alongside the trunk.
3. The subject received, using the quadripolar planar IFC technique, either 100 Hz AMF parameter or 0 Hz AMF (according to the randomization order) for 30 minutes over the lumbar area.
4. A mechanical algometer, at a constant rate pressure force of 1 $kg/cm^2/seg$, was applied to register the values of pressure pain threshold (PPT) before (M1, M2), during (M3, M4) and after (M5) the application of the second IFC protocol in the same fashion as done on the first visit. For an overall view about the experimental procedure see Figure 16.

All measurements included in the two treatment protocols were performed by the same investigator who was blinded to the type of IFC protocol treatment applied. The experimental procedure took place during daytime (between 9 AM and 5 PM), and each session took approximately 80 minutes. Both stimulation (AMF= 100Hz ; AMF= 0Hz) protocols using IFC and the measurements of pressure pain threshold were conducted in a quiet, isolated room, free of outside distractions in Corbett Hall at the University of Alberta in the Sport Therapy Research Lab.

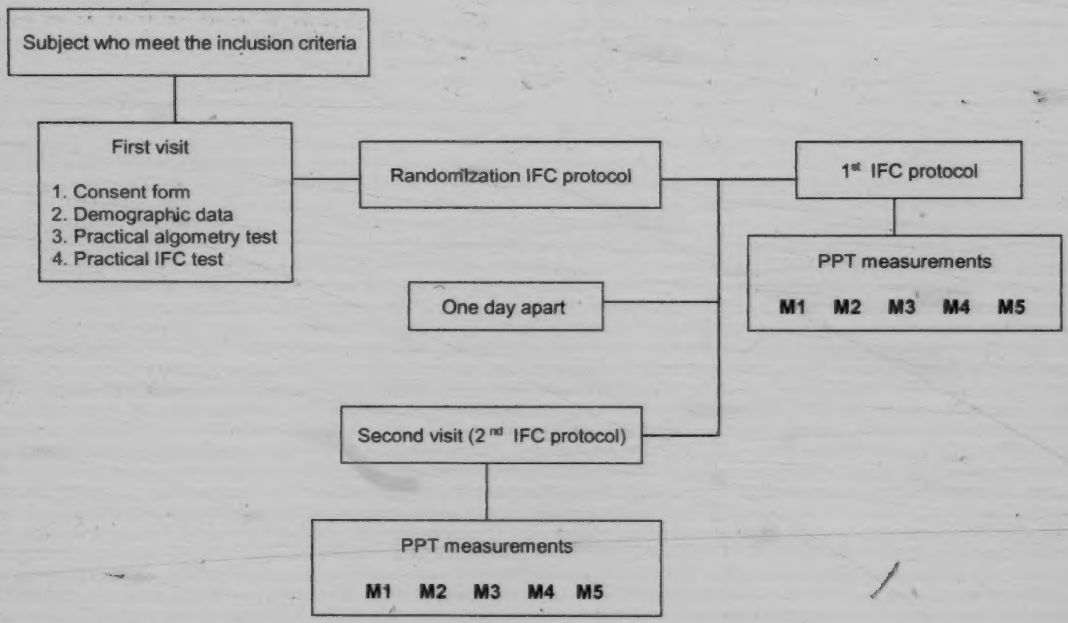


Fig. 16 Flow chart with details about sequence of the experimental procedure

3.7 STATISTICAL ANALYSIS

The data of pressure pain thresholds were analyzed descriptively (e.g. mean, standard deviation) considering each factor (AMF, gender and time). A 3 way ANOVA mixed design with repeated measures (3 independent variables; IFC protocol treatment [AMF=100 Hz, AMF= 0 Hz], gender [female, male], and time variable [before, during and after treatment]) was be used to evaluate the differences in the pressure pain threshold values (dependent variable: pressure pain threshold evoked in the area) among three conditions (before-during-after interferential current application) for females and males.

A Bonferroni's post hoc test was used to determine which variable changed more than the others (between treatments, between each treatment during the experimental procedure time course, and between genders). The level of significance was set at $\alpha = 0.05$. The SPSS Statistical Program version 11.0 (Statistical Package for the Social Sciences) was used by an external assistant to perform the statistical analysis.

The clinical significance of the results of this study was assessed retrospectively by using the distribution-based methods. Both the effect size and the standard error of measurement values were calculated to determine the minimal clinically important difference (MCID) for the pressure pain thresholds measurements.

4. CHAPTER FOUR: RESULTS

The present study examined the results of the effects of two different IFC treatment protocols (AMF= 0Hz; AMF = 100Hz) on the pressure pain thresholds among healthy volunteers. All participants were between 18 and 40 years of age. Each participant was informed of his/her rights and with full disclosure of the benefits and risks of the study.

4.1 SUBJECT CHARACTERISTICS

Forty six subjects were included in this study: twenty three females and twenty three males. The demographic descriptive statistics for all forty six subjects is listed below. Table 4-1 presents the mean and the standard deviation of height (measured in centimeters), weight (measured in kilograms) and age (measured in years) for all forty six subjects and by gender (female and male).

4.1.1 HEIGHT, WEIGHT AND AGE

Table 4.1 presents the mean and standard deviation of height, weight and age for all 46 subjects and by gender (female and male)

Table 4.1 Descriptive Statistics for Study Subjects Height, Weight and Age

Subjects	Height (m)		Weight (Kg)		Age (years)	
	Mean	SD	Mean	SD	Mean	SD
All subjects	167.783	±9.362	67.983	±12.407	29.565	±6.246
Males	174.304	±7.618	74.965	±12.106	28.522	±7.089
Females	161.261	±5.683	61.000	±8.148	30.609	±5.220

4.2 COMPARISON OF IFC PROTOCOLS (AMF= 100 Hz; AMF= 0 Hz) ON PPT VALUES DURING THE COURSE OF EXPERIMENTAL PROCEDURE (BEFORE, DURING AND AFTER)

A three- way ANOVA with repeated measures analysis was used to demonstrate that there was no significant differences ($p > 0.05$; Tables 4.2 - 4.4 ; Fig 17- 20) between the two IFC frequency treatment protocols (AMF=100 Hz ; AMF= 0 Hz) on the pressure pain thresholds (PPT) in healthy individuals.

Moreover, statistical analysis failed to show any significant interaction between IFC treatment and gender (Fig.21, 22) ($p = 0.399$), measurement and gender ($p = 0.90$), IFC treatment, measurements and gender ($p = 0.106$) IFC treatment and measurements ($p = 0.836$). This implies that regardless of the gender or the treatment protocol applied, the PPT will not change over time. The only significant ($p = 0.00$) main effect was in the time of PPT measurements (ES = 0.479, observed power 0.99). This suggest that pressure pain threshold did change at particular IFC application times (10 minutes before treatment, time 0, 15 minutes into treatment, 30 minutes of treatment, and 30 minutes post treatment).

The effect sizes (ES) (Partial Eta Squared) (Table 4.2) obtained for the IFC treatment main effect and interactions such as IFC treatment and gender, measurement and gender, IFC treatment, measurements and gender, and IFC treatment and measurements were very small ranging from 0.000 to 0.174, demonstrating a very minimal impact for the variables mentioned previously on the PPT values. This was particularly noticeable in the minimum observed power achieved (0.000) for IFC treatment (see Table 4.2) Therefore, according to the values of ES and observed power, it can be conclude that there was no significant difference between the application of two IFC treatment protocols in modifying the pressure pain thresholds (PPT) in healthy females and males ($p = 0.926$).

Table 4.2 Summary Table for Repeated Measures Analysis

Effect		Value	F	Partial Eta Squared	Hypothesis df	Error df	Significance	Observed Power[a]
IFC treatment	Wilks' Lambda	1.000	0.009	0.000	1	44	0.926	0.051
IFC treatment / Gender	Wilks' Lambda	0.984	0.073	0.016	1	44	0.399	0.132
PPT measurements	Wilks' Lambda	0.521	9.407	0.490	4	41	0.000*	0.999
PPT measurements / Gender	Wilks' Lambda	0.826	2.163	0.174	4	41	0.900	0.587
IFC treatment / PPT measurements	Wilks' Lambda	0.966	0.360	0.034	4	41	0.836	0.124
IFC treatment / PPT measurements / Gender	Wilks' Lambda	0.834	2.046	0.166	4	41	0.106	0.560

* Significant ($p < 0.05$)

[a] Post-Hoc (observed) power is calculated by considering the observed differences in means, the standard error and sample size.

Table 4.3 Test of between subjects effect

Source	Sum of Squares	df	F	Significance	Partial Eta Squared	Observed Power
Gender	4.305	1.000	0.107	0.745	0.002	0.062

Table 4.4 Recorded pressure pain thresholds (Kg/cm2/sec) for both IFC protocols (AMF=100 Hz; AMF= 0 Hz) and for gender during the experimental procedure time course (mean ± SD)

	M1 Pre-treatment (-10 min)	M2 Pre-treatment (0 min)	M3 During treatment (15 min)	M4 During treatment (30 min)	M5 Post-treatment (60 min)
AMF 100HZ Female	5.9478 ± 1.9	6.3696 ± 2.3	6.9913 ± 2.6	6.9870 ± 2.5	6.0913 ± 2.1
AMF 100HZ Male	6.1870 ± 2.3	6.2522 ± 2.0	6.9217 ± 2.6	6.6957 ± 2.2	6.5217 ± 2.5
AMF 0HZ Female	5.7522 ± 1.4	6.1043 ± 1.6	6.9609 ± 2.1	6.6957 ± 2.1	6.1826 ± 1.4
AMF 0HZ Male	6.2261 ± 2.1	6.5435 ± 2.5	6.8739 ± 2.4	6.9913 ± 2.4	6.8043 ± 2.6

Fig. 17 Main effect of IFC treatment protocols (AMF= 100 Hz; AMF= 0 Hz) on PPTs for healthy female and male subjects

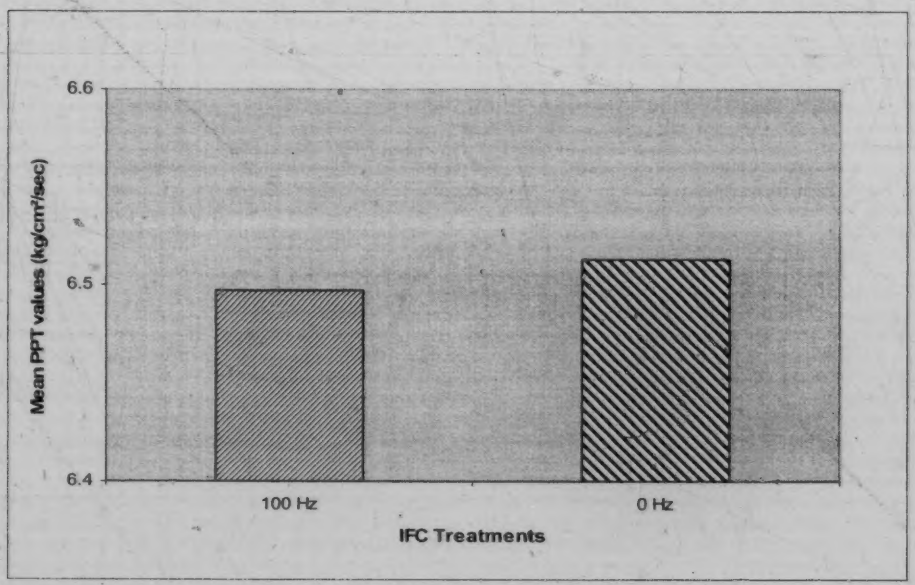


Fig. 18 Summary of averaged PPT difference scores for gender and for IFC treatments plotted against the time course of the experiment. Effects of gender and treatments on PPT measurements did not reach statistical significance ($p > 0.05$)

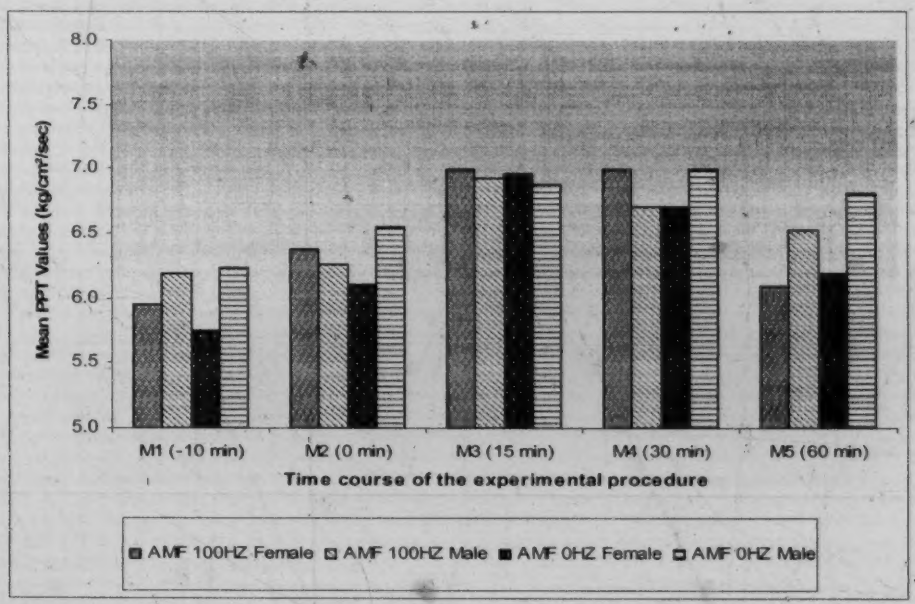


Fig. 19 Mean change in pressure pain thresholds ($Kg/cm^2/sec$) for healthy females receiving two IFC treatments (AMF= 100Hz; AMF= 0Hz)

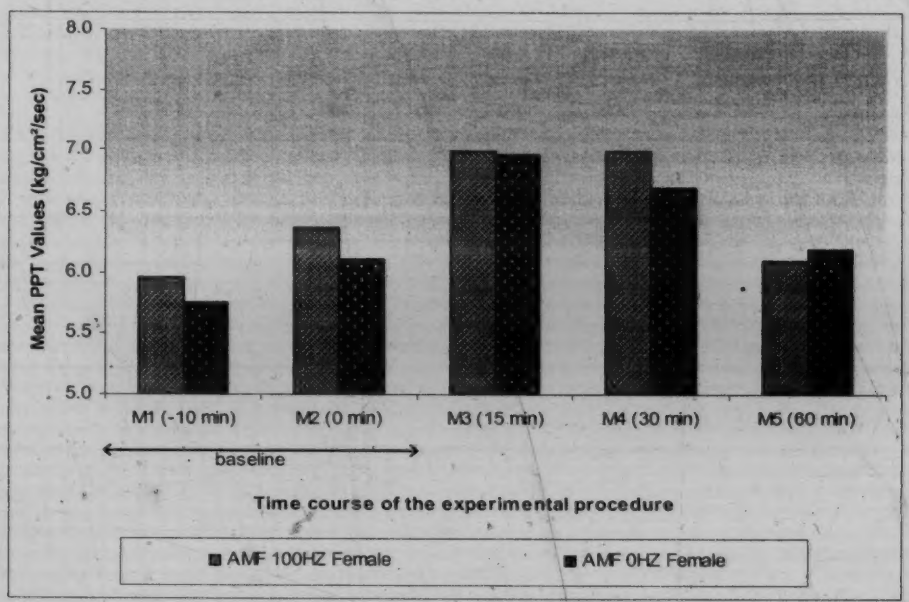


Fig. 20 Mean change in pressure pain thresholds ($Kg/cm^2/sec$) for healthy males receiving two IFC treatments (AMF= 100Hz; AMF= 0Hz)

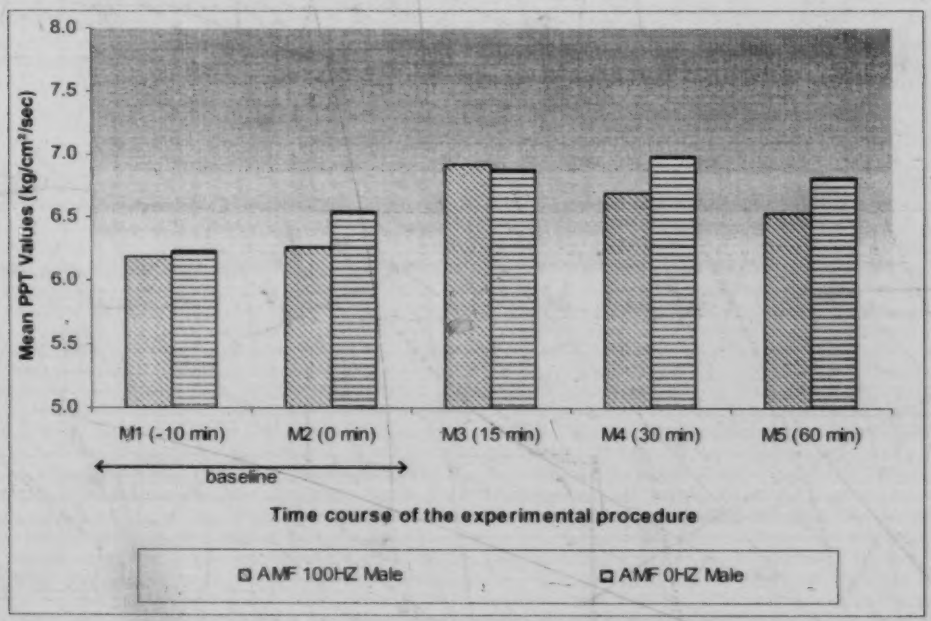


Fig. 21 Gender differences in pressure pain thresholds ($Kg/cm^2/sec$) for the first IFC protocol treatment (AMF= 100Hz)

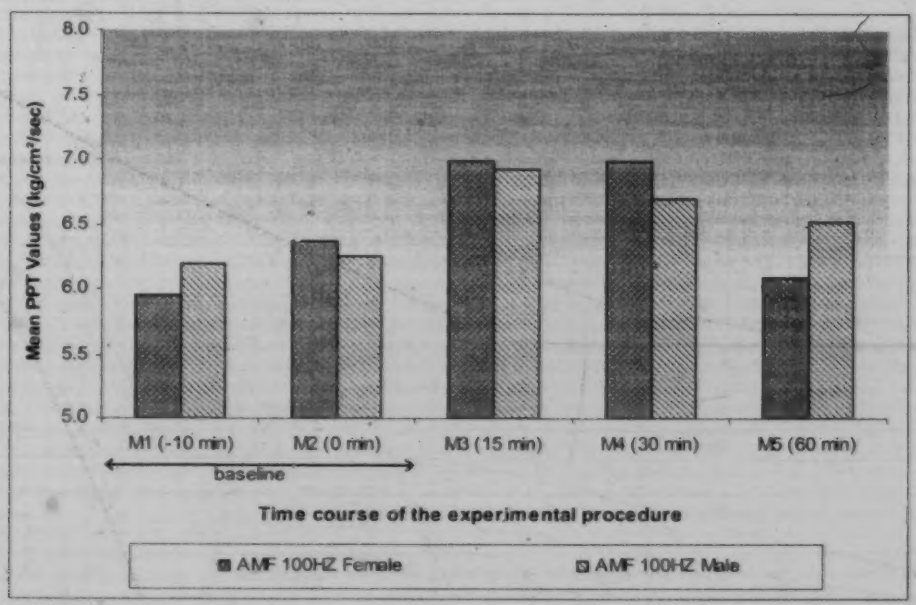
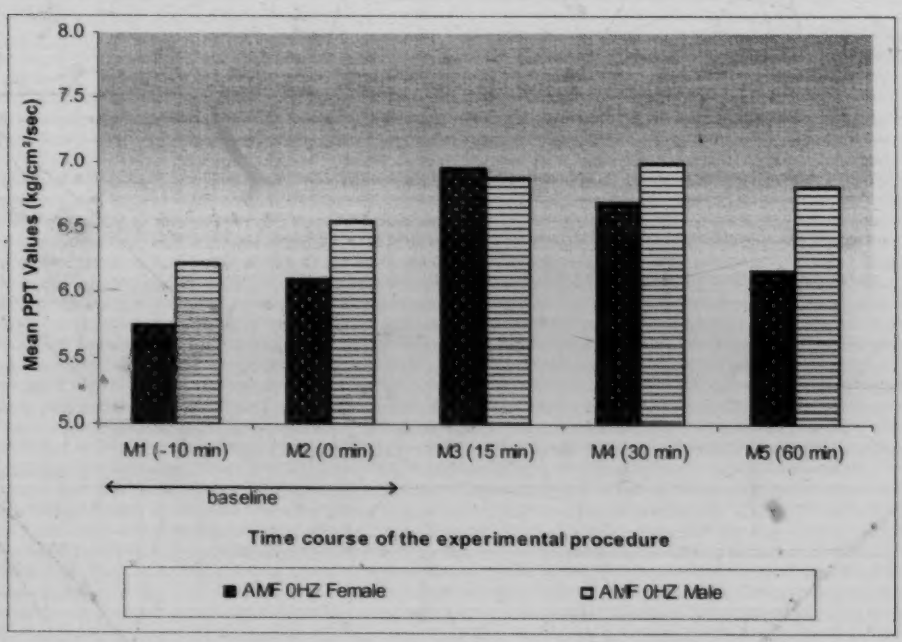


Fig. 22 Gender differences in pressure pain thresholds (kg/cm^2/sec) for the second IFC protocol treatment (AMF= 0Hz)



4.3 COMPARISON BETWEEN DIFFERENT PPT MEASUREMENTS DURING THE TIME COURSE OF THE EXPERIMENTAL PROCEDURE.

A three-way ANOVA with repeated measures analysis showed that there were statistical differences (p= 0.00) among the different PPT measurements during the time course of the experiment (Tables 4.5 and 4.6; Figure 23). Interestingly, although marginal, there were significant differences between M1 (10 minutes before treatment) and M2 (Time 0). It is possible that the increase in the PPT values observed between the first (M1) and the second (M2) measurement could have been attributed to psychological mechanisms of expectancy for pain relief among subjects. These results justify the inclusion of a second measure before IFC treatment, because the two were different. More relevant, significant differences were obtained ($p < 0.05$) between M1 (10 minutes before treatment) and M3 (15 minutes of treatment). Similarly, significant differences occurred between M1 (10 minutes before treatment) and M4 (30 minutes of treatment). On the other hand, statistical analysis failed to show any significant difference between M1 (10 minutes before treatment) and M5 (30 minutes post treatment). In this case, PPT values tended to return towards those displayed at baseline.

Table 4.5 Descriptive statistics for the main effects

Measurements	Mean	Std. Error	95% Confidence Interval	
			Lower Boundary	Upper Boundary
M1 (-10 min)	6.028	0.267	5.491	6.565
M2 (0 min)	6.317	0.293	5.726	6.908
M3 (15 min)	6.937	0.336	6.260	7.614
M4 (30 min)	6.842	0.321	6.196	7.489
M5 (60 min)	6.400	0.310	5.776	7.024

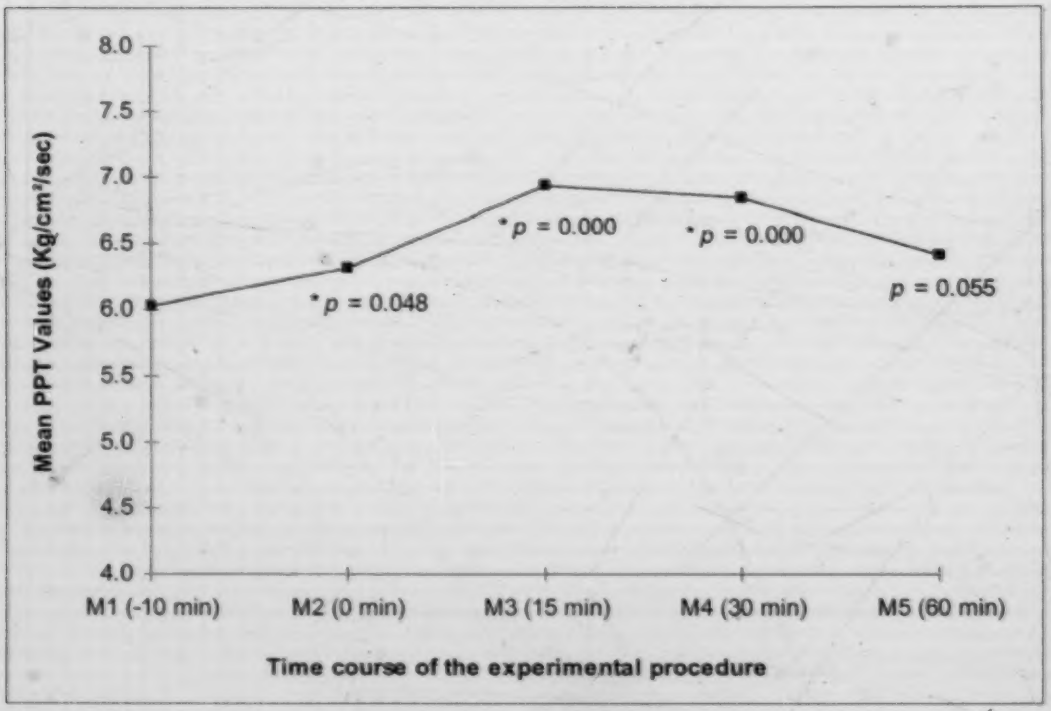
Table 4.6 PPT measurement differences over time

Reference measurement (R)	Comparative measurement (C)	Mean difference (R-C)	Std. Error	Sig.[a]	95% Confidence Interval for difference[a]	
					Lower Boundary	Upper Boundary
M1 (-10 min)	M2	-0.289*	0.097	0.048	-0.576	-0.002
	M3	-0.909*	0.162	0.000	-1.388	-0.430
	M4	-0.814*	0.170	0.000	-1.316	-0.312
	M5	-0.372	0.127	0.055	-0.748	0.005
M2 (0 min)	M1	0.289*	0.097	0.048	0.002	0.576
	M3	-0.620*	0.115	0.000	-0.959	-0.280
	M4	-0.525*	0.137	0.004	-0.929	-0.121
	M5	-0.083	0.120	1.000	-0.437	0.272
M3 (15 min)	M1	0.909*	0.162	0.000	0.430	1.388
	M2	0.620*	0.115	0.000	0.280	0.959
	M4	0.095	0.084	1.000	-0.154	0.344
	M5	0.537*	0.103	0.000	0.233	0.841
M4 (30 min)	M1	0.814*	0.170	0.000	0.312	1.316
	M2	0.525*	0.137	0.004	0.121	0.929
	M3	-0.095	0.084	1.000	-0.344	0.154
	M5	0.442*	0.117	0.005	0.096	0.789
M5 (60 min)	M1	0.372	0.127	0.005	-0.005	0.748
	M2	0.083	0.120	1.000	-0.272	0.437
	M3	-0.537*	0.103	0.000	-0.841	-0.233
	M4	-0.442*	0.117	0.005	-0.789	-0.096

* : The mean difference is significant at the 0.05 level.

[a] : Adjustment for multiple comparisons: Bonferroni

Fig. 23 Descriptive statistics for the main effect: PPT Measurements differences during the time course of the experimental procedure. * Significant differences ($p = < 0.05$)



4.4. CLINICAL SIGNIFICANCE

Even though there were significant differences in the pressure pain threshold values during the time course of the experimental procedure, these results failed to reach clinical significance. The increase in the pressure pain threshold calculated (0.524 kg/cm^2) was not sufficient to achieve the minimal amount of change that is considered as the minimal clinically important difference ($\geq$ 1.14 kg/cm^2).This was according to a retrospective assessment and calculations of clinical significance included in this study.

CHAPTER FIVE: DISCUSSION

Despite the profuse use of interferential current (IFC) in clinical practice, its effectiveness is controversial. The clinical literature demonstrates IFC to be either effective or ineffective, depending on the painful condition. For example, IFC has been shown to decrease pain in knee osteoarthritis (Quirk et al. 1985; Ni Chiosoig et al. 1994; Adedoyin et al. 2002, 2005; Defrin et al.2005), the ankle (Christie & Willouhby 1990) and the humerus (Martin & Palmer 2000) pain fractures, low back pain (Checchia 1991; Werners *et al.* 1999; Hurley *et al.* 2001, 2004; Adedoyin *et al.* 2005), fibromyalgia (Almeida *et al.* 2003; Raimundo *et al.* 2004) and postoperative knee pain (Jarit *et al.* 2003). In contrast, no analgesic results of IFC have been documented in soft tissue shoulder pain (Van der Heijden *et al.* 1999), and chronic jaw pain (Taylor *et al.*1987). Similarly, findings of some controlled trials using various models of inflammatory pain (Jorge *et al.* 2006) and experimentally induced pain models (Stephenson & Johnson 1995, Johnson & Wilson 1997; Johnson & Tabasan 1999, 2002, 2003; Cheing & Hui-Chan 2003; McManus *et al.*2006: Shanahan *et al.*2006), provide certain evidence to support the rationale for using IFC while others question its efficacy (Alves-Guerreiro *et al.* 2001, Minder *et al.* 2002; Stephenson & Walker 2003).

Amplitude-modulated frequency (AMF) or the "beat frequency" parameter has been traditionally considered an effective component of IFC (Wodsworth & Chanmugam 1983; Goats 1990; Kloth 1992; Low & Reed 2000). Nevertheless, this paradigm is changing. Most of the recent experimental evidence questions the importance of the AMF component in the therapeutic effects, suggesting that the modification of the AMF has a

marginal effect on the activation of physiologic responses, and advocating that the medium frequency component (4000 Hz) could be the main element in order to evoke the stimulating effects of IFC (Johnson 1999; Palmer *et al.* 1999, 2004). However, the amount of available information regarding the effects of different AMF settings or the absence of AMF on pain response is still far from be conclusive. Furthermore, the effects of the absence of AMF in IFC applications have not been completely studied. Thus, there is clearly a need to assess the pain-relieving of different AMFs of IFC, especially regarding the effect on pain modulation when using a pure 4 kHz medium frequency current (AMF=0).

The purposes of this study were 1) to investigate the hypoalgesic effects of interferential current therapy on an experimentally-induced mechanical pain model in normal subjects, and 2) to describe and compare the hypoalgesic effect of interferential current therapy on pressure pain threshold using an amplitude-modulated frequency (AMF) parameter of 100 Hz and the effect of interferential current therapy without using the amplitude-modulated frequency (AMF = 0 Hz) parameter in healthy males and females.

In order to answer these questions, this section will be divided in the following main sections: 1) the hypoalgesic effectiveness of IFC on an experimentally-induced mechanical pain in healthy male and female subjects 2) the hypoalgesic effectiveness of the amplitude-modulated frequency (AMF) 100 Hz and pure medium frequency current (AMF= 0 Hz) on the pressure pain threshold in healthy subjects, 3) PPT and gender differences, and 4) strengths and weakness of this study.

5.1 HYPOALGESIC EFFECTIVENESS OF IFC ON EXPERIMENTAL MECHANICALLY-INDUCED PAIN IN HEALTHY FEMALE AND MALE SUBJECTS

The first hypothesis of this research was: the application of interferential current therapy (IFC) will increase the pressure pain threshold during and after the application of the treatment protocol in the study group. The hypoalgesic mechanisms proposed for IFC are multiple. The increase of circulation (De domenico 1982; Savage 1984; Nikolova 1987) in the area, the physiological block of nerve conduction (De domenico 1982; Goats 1990), the activation of the descending pain suppression (De domenico 1982; Savage 1984; Goats 1990), the placebo component, and the stimulation of the gate control theory (Melzack & Wall 1965) have been primarily considered as the physiological rationale for applying IFC.

The results obtained in the present study did confirm the hypothesis that IFC can increase the pressure pain threshold (PPT) in healthy subjects compared to baseline values ($p < 0.05$, Table 4.5 and Figure 23). However, this increase on PPT was only significant during the application of IFC and no significant differences were obtained 30 minutes after IFC application. Improvement in the pressure pain threshold (PPT) values in the subjects during the application of IFC could primarily be due to the stimulation of large (Aβ) diameter fibers (gate control theory). The gate control theory (Melzack & Wall 1965) suggested that the activation of the large myelinated fibers (low threshold mechanoreceptors) subserving touch, pressure and vibration (i.e. A α and A β fibers) is thought to facilitate the pre-synaptic inhibition of the transmission cells in the dorsal horn, thus reducing pain transmission.

When only non-noxious sensory nerve fibers are excited, pain suppression is imposed by these large-diameter sensory afferents (Kloth 1991). The intensity level applied in this study produced a "pin and needles" sensation in the subjects. The application of IFC limited at sensory level, without muscle contractions, is in accordance with the activation of fast transmission Aβ (non-nociceptive) fibers. Moreover, the characteristics of pressure algometry in terms of inducing a short and much localized type pain suggest that the mechanically induced pain is not a sufficient stressor to elicit higher centre pain mediating mechanisms.

A second possible mechanism responsible of improvement in PPTs during the application of IFC could be the placebo effect rather than the action of physiological effects. The placebo effect occurs whenever a patient and a physician perceive a treatment as effective and is often prone when using technologically impressive therapies such as electrotherapy (Johnson & Tabasam 1999). It is possible that changes in pressure pain thresholds reported would have been attributed just to the act of applying the treatment rather than to the active ingredient of the treatment. Other placebo-related mechanisms potentially involved in the increase of PPT values in response to IFC could have been the psychological expectancy and the learning effect. Expectancy includes different the construct as belief, association, and it is considered a relevant component in the placebo response associated to electrotherapy (Roche *et al.* 2002). For example, psychological mechanisms expectancies for pain relief produced significant increase in the ischemic pain threshold (Roche *et al.* 2002), and reduced the pain intensity in an electrical pain model (Montgomery and Kirsch 1997).

On the other hand, the application of repetitive mechanical stimuli (algometry) over a period of time could have triggered a learning effect (familiarization) in the subjects, requiring more pressure to reach the mechanical threshold (increased PPT value).

The placebo effect of IFC has been studied previously under experimentally induced pain conditions (Stephenson & Johnson 1995; Johnson & Tabasan 1999; Stephenson & Walker 2003) as well as clinical settings (Taylor *et al.*1987; Van der Heijden *et al.* 1999; Adedoyin *et al.* 2002; Jarit *et al.* 2003; Defrin *et al.* 2005; Al-Abdulwahab *et al.* 2006). For example, Adedoyin *et al.* (2002), when investigating osteoarthritis pain, allocated 30 patients alternatively into IFC or placebo groups. Pain ratings in the IFC group were found to be significantly better than for the placebo group. Similarly, Defrin *et al.* (2005) showed that IFC applied to the knee significantly reduced both chronic pain intensity and stiffness and significantly increased pain-free ROM in the knee when compared with a placebo group. In post operative knee pain, Jarit *et al.* 2003, reported the favorable effects of IFC on pain. Other studies concluded that IFC significantly modified (increased the threshold) a person's response to experimentally-cold induced pain in healthy subjects when compared with a sham application (Stephenson & Johnson 1995; Johnson & Tabasam 1999; Tabasan & Johnson 1999).

Other authors have concluded, however, that a placebo had a major influence on the IFC analgesic response. Thus, Van der Heijden *et al.* (1999) reported no significant differences in functional status (SQD), pain (VAS) and ROM at six weeks of treatment and at intervals up to one year between the active and placebo groups for soft tissue shoulder pain. In addition, Taylor *et al.* (1987), after applying three 20 minute sessions

each with a sweep frequency of 90-100 Hz at comfortable intensity stimulus to patients, concluded that there was no statistically significant difference in the pain assessed by a 10-cm VAS and jaw opening (ROM) between the treatment and placebo groups. Similarly, the analgesic effects of IFC in experimentally cold-pressor pain in healthy subjects were evaluated, and it was found that IFC did not significantly alter the pain threshold (Stephenson & Walker 2003). Moreover, Minder *et al.* (2002) concluded that the application of IFC was unable to offer clear analgesic effects compared to a control group when using the exercise experimental pain model.

Based on the information provided above, conclusive results regarding the impact and the extent of the placebo component in the analgesic response of IFC are still unclear. Although this study attempted to control the effect of the placebo component (i.e. equipment out the sight of the subject), its effects cannot be ruled out as being at least partly responsible for the PPT outcomes shown. Only the inclusion of a placebo group in the design of this study could have been useful to understand its real effects on the PPT outcome.

There are a variety of experimental pain models (e.g. heat, cold, exercise) that have been used to induce pain in healthy subjects in experimental trials. Even though pain research in clinical settings has the advantage of direct clinical relevance, experimental pain models still offer major advantages. For example, under experimental conditions, volunteers are usually used as his/her own control (repeated measures design) thus minimizing inter individual response variation, and variation over time (Arendt-Nielsen & Sumikura 2002). Also, when using experimentally-induced pain models, both the elicited experimental pain and the noxious stimulus produced (intensity, location) are

under direct control of the investigator and can be systematically manipulated and standardized (Wolff 1984). These conditions can be hardly achieved in clinical research settings. Clinical pain is highly confounded by several variables (e.g. cognitive, psychological, social) involved in both acute and chronic painful conditions. All the aforementioned factors can contribute to increased variability in patient responses in clinical pain. Experimental pain models can thus be a useful tool to help guide subsequent clinical trials.

Many attempts have been made to test the effectiveness of IFC in experimentally induced pain. These studies include the use of both endogenous (i.e. exercise) and exogenous (e.g. heat, pressure) experimental pain models. Pressure algometry is the most common modality used to apply a uniform rate of pressure for inducing experimental mechanical pain. The algometry and the assessment of pressure pain thresholds have been widely and successfully used in various trials in order to assess treatment results (Alves-Guerreiro *et al.* 2001; Farasyn & Meeusen 2003; Aspegren *et al.* 2003; Chesterton *et al.* 2003; Ylinen *et al.* 2003, 2006; McManus *et al.* 2006). The pressure pain sensitivity is the result of a combined measure of cutaneous and deep tissue mechanosensitivity. However, stimulation of thin myelinated (Aδ) and non-myelinated (C) afferent fibers from deep tissues are strongly involved in the painful sensation elicited by pressure algometry (Graven-Nielsen 2006).

An overall analysis of results of the application of IFC on experimentally induced pain provides evidence, especially consistent in cold-induced pain, to support its hypoalgesic effectiveness (Stephenson & Johnson 1995; Johnson & Wilson 1997; Tabasam & Johnson 1999; Johnson & Tabasan 1999, 2002, 2003a b; Cheing & Hui-Chan

2003; Shanaham *et al.* 2006; McManus *et al.* 2006). However, there are others studies, mainly based on other experimental models that demonstrate some level of controversy (Alves-Guerreiro *et al.* 2001, Minder *et al.* 2002; Stephenson & Walker 2003). Tabasam & Johnson (1999), in a single blind placebo controlled trial, examined the analgesic effects of IFC on cold-induced experimental pain. Results showed that 20 minutes of IFC (100 Hz) at a "strong but comfortable level" elevated the pain threshold in healthy individuals. The findings of this study disagree with a study by Stephenson & Walker (2003), finding that IFC at different AMF settings (30 Hz, 100 Hz) did not significantly alter the cold pain threshold in healthy subjects when compared to sham application . The later results are in agreement with other studies carried out using an exercise pain (DOMS) model and mechanically induced pain. Alves-Guerreiro *et al.* (2001) concluded that premoduated IFC (150 Hz) at "strong but comfortable" intensity sensation failed to show significant differences in mechanical threshold values when compared to a control group. In the same way, Minder *et al.* (2002) demonstrated that 30 minutes of IFC (10-20 Hz; 80-100Hz) had no overall beneficial effect on pain intensity in delayed onset muscle soreness compared to a control or placebo.

Thus, decisions concerning the hypoalgesic effects on experimental painful conditions are far from conclusive. More investigations are needed to clarify whether IFC has a possible differential hypoalgesic response based on the type of pain model used. The use of different experimental pain models may account for the discrepancy in findings regarding the effects of IFC. However, the study of these theoretical interactions escapes the intention and methodology of this research.

A review of literature shows that the cold-pressor model has been, by far, the most utilized modality for assessing the hypoalgesic effectiveness of IFC (Stephenson & Johnson 1995; Johnson & Wilson 1997; Tabasam & Johnson 1999; Johnson & Tabasam 1999, 2003a, b; Stephenson & Walker 2003; McManus *et al.*2006; Shanahan *et al.* 2006). The fact that a higher proportion of studies were conducted using this model can be explained by the type of pain response elicited by this technique. The cold-pressor model, as well as the ischemic model, induces a deep-seated, aching, pain sensation that resembles the experience of clinical pain. The cold-pressor model offers a stimulus consistent with contemporary multidimensional models of pain by stimulating both A delta and C fibers. This is clinically relevant because this model produces a reaction that is both "sensory-discriminative and emotive motivational" (Johnson & Tabasam 1999; Stephenson & Walker 2003). However, the cold-pressor model also has limitations. For example, its application is limited only to distal segments. Also, subjects have reported that the pattern of pain associated to this model is less preferable when compared to a short and much more localized painful stimulus (McManus *et al.* 2006).

Even though the application of mechanical stimulation has been extensively used and validated as a reliable (Orbach *et al.* 1998; Nussbaum & Downes 1998; Brennum *et al.* 1989; Orbach *et al.* 1989; 1998; Farasyn & Meeusen 2003; Prushansky *et al.* 2005; Ylinen *et al.* 2005, 2006; Potter *ét al.* 2006; Cathcart & Pritchard 2006) versatile, and convenient mode to evoke pain in experimental conditions, its application as an experimental pain model in order to test the hypoalgesic effectiveness of IFC is scarce. In this regard, only two investigations, with different results, have been conducted. Alves Guerreiro et al. (2001), in a randomized with repeated measures trial, examined the

neurophysiological and hypoalgesic effects of three types of electrical stimulation (IFC, TENS and action potential stimulation therapy-APS) on mechanical pain threshold of healthy subjects. Premoduated IFC (150 Hz) was applied over the median nerve for 15 minutes at a "strong but comfortable" intensity sensation. Outcomes included in this study included the mechanical pain threshold and the recording of compound action potentials. The authors concluded that none of the aforementioned modalities produced significant differences in mechanical threshold values when compared to a control. IFC however, produced a significant change in peak to peak amplitude when compared to TENS and APS. Conversely, McManus *et al.* (2006), in a within-subject, randomized controlled trial with repeated measures, compared the efficacy of IFC on cold and mechanically induced pain in healthy volunteers. Premodulated IFC (100 Hz) was applied between the wrist and the elbow of the non-dominant forearm of subjects. Outcomes included were VAS to measure the unpleasantness and intensity, and mechanical pain threshold and mechanical pain tolerance. The authors found that the pain threshold was the outcome most affected (increased) by IFC, when compared to pain intensity and unpleasantness, on cold and mechanical pain models. A similar percentage of change in pain threshold between the two models was documented. Also, this study emphasized that both models of pain were equally effective in investigating the effects of IFC. The mechanical model, however, was identified by subjects as less uncomfortable than the cold pain model.

In summary, the application of IFC at a "strong but comfortable" intensity level was associated with an increase in the pressure pain thresholds in both healthy females and males. This effect was observed only during the application of 30 minutes of IFC

treatment. The underlying mechanism for this hypoalgesic response appears to be the direct stimulation of large myelinated fibers (Aβ). The placebo effect, however, can not be entirely excluded. Additional research including placebo group is necessary to reach conclusive directions. Finally, experimentally induced pain studies are a valuable option for the initial evaluation of the hypoalgesic effects of IFC.

5.2 HYPOALGESIC EFFECTIVENESS OF AMF= 100 Hz AND AMF= 0 HZ ON THE PRESSURE PAIN THRESHOLD IN HEALTHY SUBJECTS

The second hypothesis of this study was that the frequency of the amplitude modulated (AMF) parameter would not influence the increase of the pressure pain threshold in the subjects in the study group. A two way ANOVA with repeated measured analysis demonstrated that there were no significant differences (p = 0.926; Table 4.2, Figure 17) between the two IFC frequency treatment protocols (AMF=100 Hz; AMF= 0 Hz) on the pressure pain thresholds (PPT) in healthy individuals.

The results obtained in the present study did confirm the hypothesis that IFC would increase the pressure pain thresholds and that the AMF component would have a marginal effect on the hypoalgesic response.

Historically, the inclusion of an AMF parameter has been considered the stimulant parameter for IFC with the medium frequency component simply acting as a carrier current bringing the AMF into the deeper tissues (De domenico 1982; Wodsworth & Chanmugam 1983; Goats 1990; Low & Reed 1990) It has been claimed that the AMF initiates mechanisms that lead to analgesia (Kloth 1991; Savage 1991). Moreover,

specific textbooks on IFC offer prescriptive treatment regimes based on different AMF selections (Nikolova 1987; Low & Reed 1990; Kloth 1991; Savage 1992; Low & Reed 2000). The rationale for applying IFC at high frequencies (100 Hz) is based on the belief that AMF settings of 100 Hz are thought to be responsible for stimulating the large diameter, fast transmission Aβ (non-nociceptive) fibers. This may result in analgesia via the pain gate mechanism (Melzack & Wall 1965). This theory however, was not in line with the results of this study since IFC without using the beat frequency (AMF= 0) could lead to increased pressure pain thresholds in healthy subjects as well (hypoalgesic effects).

The available evidence regarding the effects of AMF on the analgesic response is still elusive. Moreover, controversies exist in the literature regarding the real analgesic effects of the AMF component of IFC. It is not know whether this component claimed by classical books as the active IFC element is responsible for the physiological analgesic responses when using IFC. Therefore, one of the objectives of this study was to determine the role of the AMF component in the modulation of pain evoked by a mechanical pain model. The absence of any statistical difference between the 2 AMF settings (100Hz and 0Hz) in the pain response in the present investigation, question the importance of AMF as active component of IFC. The findings of this investigation are in accordance to previous studies (Johnson & Tabasan (1999b, 2003a; Palmer *et al.* 1999; Palmer et al. 2004; Kinnunen & Alasaarela 2004) suggesting that the medium frequency (4 kHz) component is actually a relevant stimulation parameter. In this regard, Johnson & Tabasan (1999b, 2003a) failed to find any difference in the magnitude of the elevation of a cold pain threshold or pain ratings across a range of IFC AMF (20, 60, 100, 140, 180,

and 220) of IFC in healthy subjects. They stated that experimental cold pain was not influenced by AMF frequencies. Palmer *et al.* (1999) examined the effects of altering the AMF on nerve excitation. They found no differences between pure 4 kHz current (AMF=0Hz) and interference wave (AMF= 100Hz) in the amplitude required to achieve sensory, motor and pain thresholds. Moreover, they postulated that the medium frequency component of IFC rather than the interference amplitude-modulated wave (AMF) was responsible for the recruitment of different populations of nerves. Moreover, It is been demonstrated that an AMF setting of 0Hz (pure 4000Hz current) had the same hypoalgesic profile as AMF settings of 5Hz and 100Hz (Palmer *et al.* 2004). Similarly, Kinnunen & Alasaarela (2004) investigated the sensory thresholds at different AMF settings (10Hz, 30Hz, 50Hz, and 100Hz). Because the sensory thresholds were unaffected for the different frequencies among healthy volunteers, they concluded that AMF had a minor role in sensory threshold values. These results do not support the claim that varying the AMF frequency for IFC will have differential hypoalgesic and physiological effects which is in line with the results in the present study. From the physiotherapeutic point of view, this current evidence is relevant since the selection of AMF has conventionally been the central parameter of clinical decision making with IFC.

The absence of influence of the AMF in the hypoalgesic response in this investigation suggests that more complex physiologic mechanisms for pain relief could be operating. There are many unknown phenomena concerning the interactions of IFC into the biological tissues. For example, when applying true IFC, textbooks claim that a three-dimensional "clover-leaf" pattern is created within biological tissues producing the maximum interference in the central area of the field (Wodsworth & Chanmugam 1983;

Kloth 1991; Low & Reed 1990; Selkowitz 1999). However, the distribution of electrical currents of IFC into tissues is far from simple. For example, the three-dimensional pattern has only been correlated in a homogeneous- water medium (Treffene 1983). More importantly, Demmink (1995) assessed the pattern in a more realistic (biological) medium. He concluded that the pattern created by the interference of true IFC in the tissues is uneven and unreliable questioning the claims displayed in classical textbooks. The formation of the classic clover-leaf pattern requires that the electrical impedance of the tissues be uniform. This is not possible in human biological tissues where different tissues (e.g. skin, subcutaneous fat, fascia, muscle) and their impedances will affect the areas the interference. In addition, Lambert *et al.* (1993), in a two-dimensional model of the human thigh, analyzed electrical current distribution during true IFC. They concluded that the intensity produced was not identical, so the interference was not always optimal.

All the aforementioned, combined with varying orientation of the target nerve fibers, make it difficult to know the degree and extent of fibers stimulation when IFC is applied to biological tissues.

Probably, the main role of AMF is centered in perceiving the "quality" of the current applied rather than the hypoalgesic response in IFC. The use of higher AMF settings accompanies the "pin and needles" sensation. In contrast, lower AMF settings are perceived as a "beating" or "tapping" sensation, being less comfortable for subjects. These anecdotal comments were confirmed by Martin & Palmer (1996). They reported that, using a "strong but comfortable" intensity level, subjects experienced higher AMF frequencies (50-100Hz) as more comfortable than low (5 Hz) AMF settings. Kinnunen & Alasaarela (2004), also confirmed that low frequency pulses (1-10 Hz) were more

unpleasant than the higher ones when evaluating the sensory thresholds in healthy subjects. This could suggest some ability of the nervous system to discriminate among different AMF settings (Palmer *et al.* 1999). Moreover, considering the general consensus shown in both clinical and experimental trials (Tabasam & Johnson 1999; Hurley et al. 2001; Stephenson & Walker 2003; Johnson & Tabasam 2002; 2003; Minder et al. 2002; Jarit et al. 2003; Palmer et al. 2004; Adedoyin et al. 2005; Al –Abdulwahab et al. 2006; McManus et al.2006) in using a "strong but comfortable" sensation intensity level possibly suggests that patient's report of his/her sensation level is the main criterion of the stimulation. Thus, it is possible that the AMF component has no active role in the magnitude of pain relief achieved by IFC (Johnson & Tabasam 2003). Further work would help determine whether the intensity of the current is definitely the main stimulation parameter of IFC responsible for its hypoalgesic effects.

In contrast to the results shown by Cheing &Hui-Chan (2003), in which they reported that the analgesic effects of IFC on experimental heat pain lasted up to 30 minutes after stimulation. this present study has found that IFC produced an increase in PPT values which was rapid in onset and ending, and only occurred when the equipment was switched on. The effects evaluated at 30 minutes post IFC stimulation were negligible (Table 4.4, Figure 22), suggesting the limited hypoalgesic effects once the stimulator was switched off. Thus, the hypoalgesic effects would occur during the application rather than through prolonged exposure. These findings are in accordance with early several experimental study settings (Stephenson & Johnson 1995; Johnson & Tabasam 1999a; Tabasam & Johnson 1999; 2002, 2003a; Tabasam & Johnson 1999; McManus et al. 2006; Jorge et al. 2006).

It would seem from the present evidence that the application of IFC in a discrete 20-30 minutes session would have a very restricted time effect in managing experimentally induced pain.

The consistent trend regarding the absence of long-lasting hypoalgesic effects in this study could be attributable both the hypoalgesic mechanisms and to the parameters (intensity) selected in this study. The use of the "strong but comfortable" intensity setting has been associated with the stimulation of large-diameter afferent (A β) fibers (gate control theory). This stimulation leads to a fast onset and short duration of hypoalgesia. Conversely, the use of a higher level intensity is more in accordance with the stimulation of nociceptive afferents (A δ, C) fibers causing the activation of descending pain inhibitory mechanisms and as a consequence producing a long-lasting opioid-mediated IFC hypoalgesic effects. Further research in this area is necessary to understand the influence in selecting different levels of current intensity, and the possible activation of distinct hypoalgesic mechanisms in the post treatment effects of IFC.

In summary, the present investigation was able to demonstrate that IFC was effective in increasing the PPT in healthy subjects under experimentally controlled conditions. The IFC hypoalgesic effects, however, occurred only during the application of the treatment. No effects were observed 30 minutes after the IFC protocols were finished. The results of this study provided additional evidence that question the issue that the AMF component produces differential stimulation of nerve fibers. The relative ineffectiveness of including AMF in modifying the PPTs suggests that the medium component (4 kHz) is the dominant stimulation parameter in IFC.

5.3. GENDER DIFFERENCES IN PRESSURE PAIN THRESHOLDS IN HEALTHY SUBJECTS

The literature suggests that there are sexual differences in the experience of both experimental and clinical pain. It has been reported that females exhibit greater sensibility than males in experimentally-induced cold (Johnson & Tabasam 1999), chemical (Cairns *et al.* 2001; Svensson *et al.* 2003; Gazerani *et al.* 2005) electrical (Rollman & Harris 1987) and ischemic pain (Maixner & Humphrey 1993). The magnitude of the differences varies across the stimuli. The values seem to be the largest when using both the mechanical pain model (i.e. algometry) and electrical stimulation and the smallest effects emerged for thermal stimuli (Riley *et al.* 1998). More specifically, gender differences when using the mechanical pain model are controversial. Some authors reported no gender differences in pressure pain threshold (PPT) (Vatine *et al.* 1993; Hogeweg *et al.* 1996; Farasyn & Meeusen 2002; Christidis et al. 2005). Others, however, stated that women have lower PPTs than men (Gerecz-Simon *et al.* 1989; Hogeweg *et al.* 1992; Vanderweën *et al.* 1996; Rollman & Lauterbacher 2001; Chesterton *et al.* 2003b). The mechanisms that underlie sex-related pain differences are complex, involving multiple variables. For example, the hormonal status (Iseelee *et al.* 2001; Bajaj *et al.* 2001) and variations in nociceptive and antinociceptive processing (France & Suchowiecki 1999) have been included to explain this assumption. Similarly, cultural and physiological influences are also implicated (Riley *et al.* 1998). In this regard, males are thought to have been socialized to suppress signs of pain and under-report levels of pain. For example, a study found that males reported less pain with a female experimenter than with a male experimenter (Levine & De Simone 1991). This effect was not observed for

female subjects. Another variable could include anxiety related with the experimental condition (Rollman, 1995).

The findings of this study on healthy individuals experiencing experimental mechanical pain do not support the sexual differences in mechanically induced pain. The results of this study showed that female experienced similar PPT values at baseline when compared to males. Equally important, no differences in the outcome were demonstrated between genders during the application of the IFC treatments (AMF=100Hz, AMF=0Hz).

5.4. CLINICAL SIGNIFICANCE

Often researchers use statistical significance to test the efficacy of therapeutical interventions. However, statistical significance does not reflect the magnitude of the effect and only denotes that the results or associations between tested variables did not occur by chance (Greenstein 2003). On the other hand, from a clinical standpoint, clinical significance tells us whether the results are meaningful or not. A clinically meaningful change must be large enough to be of practical importance to patients and healthcare providers (The Cochrane Collaboration).

The application of IFC in normal subjects did not produce a noticeable impact in the increase of PPTs. Based on the results of this study the change in the pressure pain thresholds of approximately 0.5 kg/cm^2 was not sufficient to be clinically significant. In this regard, previous studies have reported that a change in pressure pain thresholds greater than 1 kg/cm^2 represents a clinically relevant change between groups in

intervention studies (Fisher AA. 1990; Hong *et al.* 1993; Pratzel HG. 1998; Chesterton *et al.* 2003; Potter *et al.* 2006). These results demonstrate that the amount of pressure pain threshold change required for measuring a clinically meaningful improvement, and not simply measurement error, is more than double that the results obtained in this study. Moreover, because the two IFC protocols (AMF= 100 Hz; AMF= 0 Hz) increased the PPTs at the same degree, IFC does not appear to have any frequency dependent effect. From a clinical perspective, the application of either AMF= 100 Hz or AMF= 0 Hz would produce similar therapeutic effects without generating any differential analgesic response based on the AMF component.

The clinical implication of this study is that the clinical effectiveness of IFC remains debatable and is still unclear. IFC may have only a marginal clinical effect. However, because this study was conducted in an experimental setting, using normal subjects, the clinical significance necessarily must be established in a clinical setting, including subjects experiencing clinical pain.

Finally, contrary to the traditional understanding regarding IFC, the results of this study challenge existing beliefs and clinical practice regarding the AMF component.

5.5. STRENGTHS AND WEAKNESSESS OF THIS STUDY

5.5.1. STRENGTHS

To the best of the author's knowledge, this is the first study in assessing the hypoalgesic effects of IFC using an AMF=0 Hz in an experimentally-induced mechanical

pain model. The study of the effects of pure medium frequency current (AMF=0) in the analgesic profile of IFC is a relatively new area of study. The results of this study will contribute to the scientific available research regarding the effectiveness of the AMF component and, at the same time, stimulate the interest in studying the mechanisms underlying the hypoalgesic mechanisms associated to IFC.

In this study, both groups (female and male groups) were free of symptoms for subjects between 18 and 40 years old. The use of a homogeneous sample, along with the application of a crossover design, considering the subject as his/her own control, facilitated the comparison among measurements because the information comes from the same individual. This study also accomplished a triple blinded approach (therapist, subject and statistician). Finally, the sample size (N= 46) was large enough to reach good statistical power (0.80) making the power and external validity good features of this study.

5.5.2. WEAKNESSESS

The results obtained in this study are only applicable to the group of subjects used and the protocol used and cannot be applicable to patients, since the pain coming from experimental conditions does not include the complex and multi-factorial entity associated to clinical pain.

The results are also applicable only for the mechanically-induced pain model. Because of the different structures stimulated, onset, presentation and perception of pain on other type of experimental models of pain (e.g. cold-pressor, eccentric exercise), the hypoalgesic profile in response to the application of IFC could differ.

Algometry is a convenient and versatile mode for inducing pain. But, the skin is inevitably stimulated, thus confounding the influence of skin and muscle pain on sensory and motor responses. It would have been interesting to eliminate the contribution of skin sensations by using a local anesthetic cream before assessing the pressure pain sensitivity (Graven Nielsen et al. 1998; Kosek & Ekholm 1995; Kosek et al 1999; Laursen et al. 1997).

Not including a placebo or control group make it difficult to conclude whether pressure pain thresholds improvement was a result of the active treatment or not. The results of this study may have been influenced by other factors involved in the application of treatments. In retrospect, it would have been advisable to include a placebo group to isolate the modality effects and to allow both the researcher and patient to be confident that the treatment is producing its effects due an active component of the therapy (IFC).

5.6 CONCLUSION

Despite its short-duration effect, IFC appears to be effective in immediately increasing the pressure pain thresholds (PPT) in healthy subjects. The hypoalgesic effects were not influenced by the AMF frequency and gender when IFC was applied at strong but comfortable intensity without muscle contractions.

CHAPTER SIX: SUMMARY AND CONCLUSIONS

6.1 SUMMARY AND CONCLUSIONS

The purposes of this study were 1) to investigate the hypoalgesic effects of interferential current therapy (IFC) on an experimental mechanically-induced pain model in normal subjects, ,and 2) to describe and compare the analgesic effect of interferential current therapy on pressure pain threshold using an amplitude-modulated frequency (AMF) parameter of 100 Hz, and the effect of interferential current therapy without using the amplitude-modulated frequency (AMF = 0 Hz) parameter in healthy males and females.

Based on the results of this study, the following conclusions can be stated:

1. The application of IFC in this study was associated with an increase in the pressure pain threshold in healthy female and male volunteers under experimentally controlled conditions.
2. No differences in gender, regarding the hypoalgesic responses of IFC, were found.
3. The inclusion of the AMF parameter does not appear to play a significant role in the IFC hypoalgesic responses. The results of this study showed that pressure pain thresholds were increased to the same extent when using AMF 100Hz and when pure medium frequency (4 KHz), or AMF=0Hz, was applied to the subject. Thus, other mechanisms, different than those

generally accepted, must be the responsible for the hypoalgesic effects associated to IFC.

4. The greatest hypoalgesic effects of IFC were present at the time of application (15 minutes) rather than through prolonged exposure. The post treatment effects of IFC were absent, with pressure pain thresholds reached similar values to baseline data.

5. The most feasible mechanism underlying the hypoalgesic effects in this study appear to be the stimulation of low threshold mechanorreceptors (A β) during the IFC treatment (see pages 72, 73). Other mechanisms, such as pain descending suppression or increased circulation (see pages 36, 37) appear to be questionable since the IFC treatment protocols used in this study included a strong but comfortable current intensity.

6. This study has highlighted the importance of laboratory-based studies. Pain laboratory studies are valuable in the initial evaluation of the analgesics effects of electrotherapy modalities. This, however, should be extended into clinical randomized-controlled trials to confirm the clinical effectiveness of IFC for pain management.

6.2 CLINICAL RELEVANCE

The use or the potential overuse of some therapeutic modalities without a strong scientific validation is a relevant issue today. The application of sensory stimulation in the form of electrical currents as a non-pharmacological alternative to control painful

conditions is a regular therapeutic tool used by physical therapists. Despite the widespread use of IFC, however, there is still a lack of objective evidence that supports its analgesic effect.

In the vast majority of cases, pain is the most recurrent complaint of patients, a good understanding of the fundamentals of hypoalgesic effects and the correct selection of stimulation parameters of electrotherapeutic modalities is crucial to achieving the best therapeutic effects. For this reason, this study was primarily focused on examining the hypoalgesic effects of a frequently used electrotherapeutic modality (interferential current therapy) and also evaluating its hypoalgesic effects using different parameters of stimulation in healthy subjects under controlled conditions. The clinical implications for this research are that IFC may be useful clinically for pain relief as this study has shown that it can elevate the pressure pain thresholds in healthy volunteers. In addition, the inclusion of AMF parameter does not appears to play a significant role in the IFC hypoalgesic responses.

This research focused only in normal subjects in controlled conditions. Because pain elicited in laboratory or experimental conditions is different when compared with clinical pain, future studies are necessary including clinical painful conditions affecting patients. Because this study did not include a placebo group, it is possible that changes in PPTs reported in this study could have been attributed to the act of applying the treatment rather than to the active ingredient of the treatment. Only the inclusion of a placebo group in the design of this study could have been useful to fully understand its real effects on the pain modulation. This could allow for greater expansion of this topic as well as improving the knowledge in this area. .

Finally, it is relevant that physical therapists, when considering analgesic treatment regimes for patients, integrate knowledge gained through their clinical experience as well as objective clinical and experimental evidence in order to improve existing clinical practice. Particularly, with IFC, physical therapists must get involved with the current evidence regarding its hypoalgesic effectiveness in both clinical and experimental settings. Most importantly, the paradigm shift concerning the role of the AMF in the hypoalgesic response component should be incorporated into the clinical decision making about IFC.

6.3 SUGGESTIONS FOR FUTURE INVESTIGATIONS

Some directions for future investigations would be:

1. To investigate the effectiveness of IFC with different settings of AMF, including AMF=0, in a placebo or control group design.

2. To investigate the effectiveness of pure medium frequency (AMF=0) IFC in different experimental pain models. For example, to determine the magnitude of the hypoalgesic response in painful conditions which resemble more closely the pain coming from clinical conditions (endogenous pain models).

3. Investigate the effects of different AMF settings of IFC in clinical painful conditions such as acute or chronic pain.

4. Study the effects of different stimulation stimulus (motor or pain level) on mechanical experimental pain models.

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Appendix 1

Advertising to recruit subjects

UNIVERSITY OF ALBERTA

Faculty of Rehabilitation Medicine
Department of Physical Therapy

"Analgesic Effects of Interferential Current Therapy on Experimental Pressure Pain Threshold (PPT) in Healthy Subjects"

WANTED

Are you healthy? Are you between 18 and 40 years old? We invite you to participate in our study. We are trying to evaluate the pain-relieving effect of electrotherapy in healthy subjects with no back problems. This study will contribute and strengthen the knowledge of electrotherapy in the treatment of painful conditions. You will need to attend 2 sessions of 80 min- in one day with at least 1 day between each session. If you wish participate or find out more information call 492-4824, or send an e-mail to Jorge Fuentes (jorgef@ualberta.ca)

Thank you in advance.

Appendix 2

Exclusion criteria questionnaire

Clinical pathology (specially in low back) Are you taken any analgesic (pain) medication?	**(yes)** **(no)** **(yes)** **(no)**
Contraindications of IFT * : a) Do you have a pacemaker?	**(yes)** **(no)**
b) Do you have abnormal skin sensation?	**(yes)** **(no)**
c) Are you pregnant?	**(yes)** **(no)**
d) Do you have metal implants in the area of stimulation?	**(yes)** **(no)**
e) Do you have epilepsy?	**(yes)** **(no)**
f) Have you ever had cancer?	**(yes)** **(no)**
g) Do you have a cardiac disease?	**(yes)** **(no)**

* From: Martin, D, and Palmer S. (2002) Chapter 18: Interferential current for pain control. In Kitchen S. *Electrotherapy evidence-based practice*. 11th ed. Churchill Livingstone.

Comments:.....
.....
.....

Appendix 3

Subject consent form

UNIVERSITY OF ALBERTA

Title of Project: Analgesic effects of Interferential Current Therapy on Experimental Pressure Pain Threshold (PPT) in Healthy Subjects **Part 1: Researcher Information**		
Principal Researcher and Academic Advisor: Dr. David Magee Affiliation : Physical Therapy Contact Information: (780) 492-5765 Name of Co- Investigator: Jorge Fuentes. Affiliation: Graduate Student, Department of Physical Therapy Contact Information: : (780) 492-4824 Email: jorgef@ualberta.ca		
Part 2: Consent of Subject		
	Yes	**No**
Do you understand that you have been asked to be in a research study?		
Have you read and received a copy of the attached information sheet?		
Do you understand the benefits and risks involved in taking part in this research study?		
Have you had an opportunity to ask questions and discuss the study?		
Do you understand that you are free to refuse to participate or withdraw from the study at any time? You do not have to give a reason without penalty.		
Has the issue of confidentiality been explained to you? Do you understand who will have access to your records/information?		
Part 3: Signatures		
I have read the information sheet and this study was explained to me by: _____ Date: _____		
I agree to take part in this study. Signature of Research Participant: _____ Printed Name: _____		
Witness (if available): _____ *Printed Name:* _____		
I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate. *Researcher:* _____ *Printed Name:* _____ _____ ** A copy of this consent form must be given to the subject.*		

Appendix 4

Data collection sheet

Subject data

ID
Gender
Age
Weight
Height
PPT practice test value

Experimental procedure data

A IFT protocol

	1st measurement	2nd measurement	3rd measurement	Mean
M1				
M2				
M3				
M4				
M5				

B IFT protocol

	1st measurement	2nd measurement	3rd measurement	Mean
M1				
M2				
M3				
M4				
M5				

Date :
Comments :

Appendix 5

Interferential therapy equipment (Chattanoga Intelec legend Stim.)

Technical specifications

Technical Specifications For Interferential Current

Output Channels: 1- 2

Amplitude: 0-50 mA RMS into a 500 ohm load

Current Limit: 50 mA RMS

Voltage (max.): 200 Volts Peak to Peak

Carrier Frequency: 5000 Hz

Beat Frequencies: 0-200 Hz

Maximum RMS Current Density:

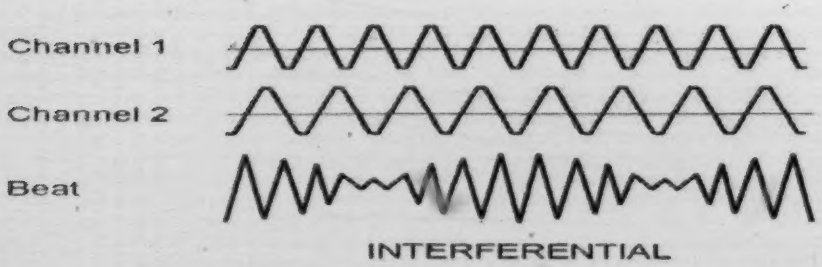
- 3" x 5" Electrode: 5.2 μA/mm²
- 2" Diameter Electrode: 24.7 μA/mm²

Maximum Power Density:

- 3" x 5" Electrode: .365 mw/mm²
- 2" Diameter Electrode: 1.74 mw/mm²

Area of Conductive Surface:

- 3" x 5" Electrode: 15 in² (9,677 mm²)
- 1 5/8"x 2" Electrode: 3.25 in² (2,0972)
- 2" Diameter Electrode: 3.14 in² (2,027 mm²)



Appendix 6

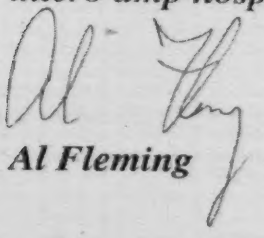
Equipment safety characteristics letter

REPORT OF LEAKAGE CURRENT FOR JORGE FUENTES ON SEPTEMBER 13, 2006 BY AL FLEMING

THE HOSPITAL STANDARD FOR LEAKAGE CURRENT IS 500 MICRO AMPS

		LEAKAGE CURRENT IN MICRO AMPS	
DESCRIPTION OF EQUIPMENT	**U of A #**	**HOT**	**NEUTRAL**
Intellect Legend Stim Chattanooga Group Inc. Serial #3129	**406698**	**20**	**100**

Note: The readings of the leakage current were taking with a BK Precision Model 1655 AC Power Supply and leakage Tester U. of A. # 162679. These devices are well under the 500 micro amp hospitals standards.



Al Fleming

Appendix 7
FPK Mechanical Algometer

http://www.paintest.com

Technical specifications

CONSTRUCTION
- Large 2 1/4" dial. Dual Graduations
- Plastic housing, stainless steel plunger and plastic crystal.

OPERATION
- Compression with 1 cm^2 (7/16") rubber tip.
- Push button maximum reading hold.
- Tension hook for accuracy check with weights.

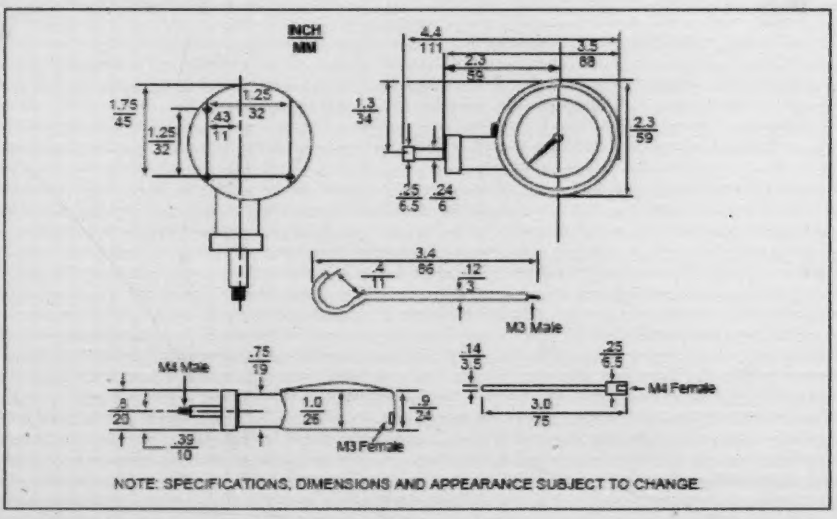
ACCESSORIES
- Rubber tip, 1 cm^2 (7/16"), 2" long hook, carrying case and manual.
- Optional pressure pad: 3" x 1 1/4".

ACCURACY
- ± 2 Grad. (thru 2500 gf), ±1 Grad. (Over 2500 gf).

WEIGHT & DIMENSIONS
- Net weight: 10 oz / 284 g.
- Overall length: 4 1/2" / 115 mm.

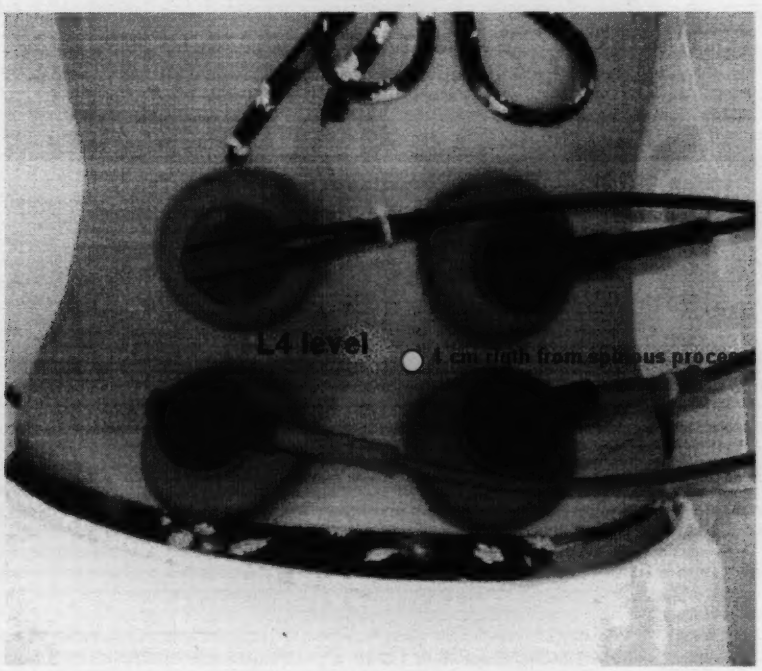
Calibration

- The device is presented with a calibration certified.
- Is calibrated with certified test weights. Periodical testing of the accuracy should be performed with test weights. The weights should be suspended on the securely mounted gage at ¼, ½, ¾ and full capacity.



Appendix 8

Interferential Current Therapy. Quadripolar technique, electrode placement and the landmark for the pressure pain threshold assessment.



Appendix 9

Information letter to subjects

UNIVERSITY OF ALBERTA

Title of the research project:
"Analgesic effect of Interferential Current Therapy on Experimental Pressure Pain Threshold in Healthy Subjects"

Researchers:

Dr. D. Magee, Professor in the Department of Physical Therapy, Faculty of Rehabilitation Medicine at the University of Alberta. 1-39 Corbett Hall. Phone (780-492-5765).

Jorge Fuentes, Master in Science student at the University of Alberta. Phone (780-492-4824)

Purpose/ Background:

Pain is by far the most common complaint of patients. Interferential current is a type of electrical current used by physical therapists in the management of pain. Despite its popularity, there is a lack of understanding on what effect this special electrical current has. The purpose of this study will be to evaluate whether this current will change pain in healthy subjects.

Procedure:

If you agree to participate, you will be asked questions to make sure you meet the criteria to be included in this study. If you meet the criteria, you will be asked your age. Similarly, your height and weight will be measured. You will be asked to attend the laboratory on two different times. The first visit will be used 1) to record personal data. 2)

To determine the type of treatment you will receive first. 3) To apply the first treatment. Moreover, you will be shown how the instrument (algometer) that is used to produce pain works. This instrument will register the amount of pressure needed to cause your first sensation of pain. It will be applied to your forearm until you understand the sensation that you are being asked to feel. At the same session, you will be given a chance to feel the strength of the current to be used. You will receive two different current treatments on the two visits. Each visit will be at least 2 hours apart. The treatment you start will be determined by "drawing out of a hat". Once the preparation stage is complete, the first treatment will be applied. For the treatment, you will lie facing down with your arms relaxed alongside the trunk. Then, four electrodes will be placed in your lower back area. The treatment will be applied for 30 minutes. During the treatment, you will feel a comfortable "pins and needles sensation". If you feel anything different than this, please tell the researcher right away. The application of the electrical current will cause no injury.

During the treatment, your pain threshold on your lumbar area will be assessed using the algometer. You will be asked to say "stop" as soon as you feel a clear sensation of pain. At this point, the algometer will be removed. The pressure will be recorded. Your pain threshold will be tested three times at five different time periods during the procedure. The first assessment will be 10 minutes before starting the treatment. The second right before the treatment has started. The third and fourth will occur during the treatment. The fifth assessment will be 30 minutes after the treatment.

The second attendance, at least 1 day after the first visit, will start with the assessment of your normal skin sensation again. You will then receive the second treatment for 30 minutes. The same three measurements of your pain threshold at five different time intervals will be taken.

Benefits/risks:

There is not personal benefit for you as participant in this study. The benefit of having you take part in this study is that you can help us to determine the pain relieving effects of this electrical therapy. There are no known risks related to the procedure itself.

Privacy/confidentiality:

All data will be kept private, except where codes of ethics or the law requires. The data you give will be kept for at least 5 years after the study is completed. The data will be kept in a safe, secure area. Your name or any other identifying data will not be attached to the data you generate by your test. Your name will never be used in any presentation or publications related of the study results. The data gathered for this study may be looked at again in the future to help us answer other study questions. If so, an ethics board will first review the study to ensure that the data are used ethically.

Freedom to withdraw:

Your participation is completely voluntary. If, at any time, you decided to withdraw you are completely free to do so without consequences.

Contact information;

If you have any questions or concerns regarding the study, procedures and your rights as a research subject, please feel free to contact Dr. Paul Hagler, phone(492 9674), Associate Dean-Research in The Faculty of Rehabilitation Medicine. If you have any questions regarding the study you can contact Mr. Fuentes, phone (492-4824) or Dr. David Magee, phone (492-5765).